Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Status:	Draft Final Amended Report for Panel Review
Release Date:	February 10, 2023
Panel Meeting Date:	March 6-7, 2023

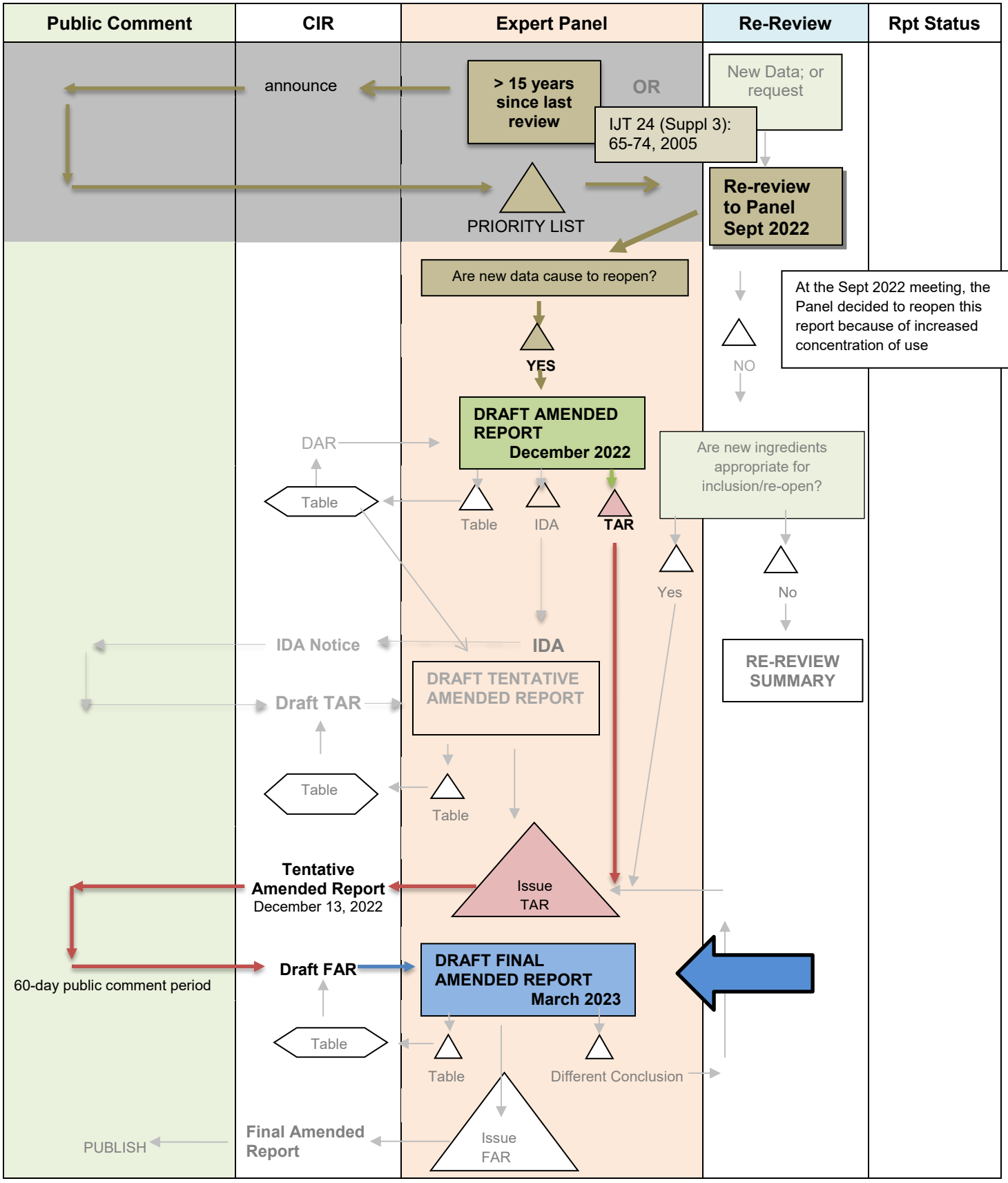
The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; and Susan C. Tilton, Ph.D. 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,

1620 L Street, NW, Suite 1200 ◊ Washington, DC 20036-4702 ◊ ph 202.331.0651
cirinfo@cir-safety.org

RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Octyldodecyl Stearoyl Stearate

MEETING March 2023



Commitment & Credibility since 1976

Memorandum

To: CIR Expert Panel Members and Liaisons
From: Regina Tucker, MS, Scientific Analyst/Writer CIR
Date: February 10, 2023
Subject: Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Enclosed is the Draft Final Amended Report on the Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics. (It is identified in this report package as *report_OctyldodecylStearoylStearate_032023* in the pdf document). At the December 2022 meeting, the Expert Panel for Cosmetic Ingredient Safety (Panel) issued a Draft Tentative Amended Report for public comment with the conclusion that Octyldodecyl Stearoyl Stearate is safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating.

As per the Panel's request at the December 2022 meeting, an updated use table format has been implemented. The frequency and concentration of use is presented both cumulatively by likely duration and exposure and individually by product category.

No new data were received or found. Comments on the Tentative Amended Report that were provided by the Council *(PCPCcomments_OctyldodecylStearoylStearate_032023)*, as well as CIR response to these comments *(response-PCPCcomments_OctyldodecylStearoylStearate_032023)* are included in this packet.

Also included in this package for your review are the report history (*history_OctyldodecylStearoylStearate_032023*), flow chart (*flow_OctyldodecylStearoylStearate_032023*), literature search strategy (*strategy_OctyldodecylStearoylStearate_032023*), data profile (*dataprofile_OctyldodecylStearoylStearate_032023*), the initial (*originalreport1_OctyldodecylStearoylStearate_122022*) and amended report of Octyldodecyl Stearoyl Stearate (*originalreport2_OctyldodecylStearoylStearate_122022*), the minutes from all the past meetings at which Octyldodecyl Stearoyl Stearate was originally discussed (*originalminutes_OctyldodecylStearoylStearate_122022*), and transcripts from the previous meetings at which this amended report has been discussed (*transcripts_OctyldodecylStearoylStearate_032023*).

The Panel should carefully consider the Abstract, Discussion, and Conclusion presented in this report. If these are satisfactory, the Panel should issue a Final Amended Report.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

FROM: Alexandra Kowcz, MS, MBA
Industry Liaison to the CIR Expert Panel

DATE: January 4, 2023

SUBJECT: Tentative Amended Report: Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics (release date: December 13, 2022)

The Personal Care Products Council respectfully submits the following comments on the tentative report, Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics.

Cosmetic Use, Table 1 and 2 – Please use a date when describing the use information rather than the word "current". The use information will not be "current" by the time the CIR report is published. Please correct this in the text of the Cosmetic Use section and the titles of Tables 1 and 2 (if both are left in the report).

Summary – In the Summary, it would also be helpful to state that the 2005 report should be consulted for additional studies that support the safety of Octyldodecyl Stearoyl Stearate. This report just summarizes new information.

Draft Report Comment Responses

Octyldodecyl Stearoyl Stearate – March 2023-Regina Tucker	
Comment Submitter: Personal Care Products Council **Date of Submission: January 4, 2023**	
Comment	**Response/Action**
(1) Cosmetic Use, Table 1 and 2 – Please use a date when describing the use information rather than the word "current". The use information will not be "current" by the time the CIR report is published. Please correct this in the text of the Cosmetic Use section and the titles of Tables 1 and 2 (if both are left in the report).	Addressed
(2) Summary – In the Summary, it would also be helpful to state that the 2005 report should be consulted for additional studies that support the safety of Octyldodecyl Stearoyl Stearate. This report just summarizes new information.	Addressed

Octyldodecyl 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: Octyldodecyl 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).

December 2022-The Expert Panel issued a Tentative Amended Report for public comment with the conclusion that Octyldodecyl Stearoyl Stearate is safe when formulated to be non-irritating as described in the safety assessment. Data from the original assessment indicated an eyeliner formulation containing 7.5% Octyldodecyl Stearoyl Stearate was moderately irritating to the eye. Accordingly, formulators should be aware of this potential and ensure that products containing this ingredient should be formulated to be non-irritating.

Octyldodecyl Stearoyl Stearate Data Profile* – March 2023 – 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 sterate. 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 2022 PANEL MEETING-REREVIEW CONSIDERATION

Belsito's Team Meeting –December 5, 2022

DR. BELSITO: So now we're going to Octyldodecyl Stearoyl Stearate. So, this is a draft-amended report on Octyldodecyl Stearoyl Stearate as used in cosmetics. In our initial assessment of this, we found the data were

insufficient to determine safety and there was a final report in 2001 on that. But subsequently, we looked at it and thought that it was sufficient in 2005.

In September of 2022, we decided to reopen this because of updated usage data with a significant increase in the concentration of use. And so, we're looking at this again. We're also being asked about the tables that we prefer.

Since the September meeting, we've got unpublished data on lip balm at 28 percent Octyldodecyl Stearoyl Stearate and an RIPT on 21 percent of the Octyldodecyl Stearoyl Stearate. And that maximum concentration of use --

DR. SNYDER: 18.5.

DR. BELSITO: -- is 18.5. So there is low dermal penetration of these, but we have no DART or chronic oral, and it's 28 percent in the lipstick. Does this bother you?

DR. SNYDER: No.

DR. BELSITO: Okay.

DR. SNYDER: I mean, I thought the most important thing was the sensitization data. You know, we're at 21 percent, 18.5, it's not absorbed. We do have some acute 14-day tox data. There's no signal there, so I was fine with it.

DR. BELSITO: Right. That was my only question. So, basically, safe as used when formulated to be non-irritating given some of the eyelid studies at 7.5 percent. Are you fine with that conclusion?

DR. SNYDER: Yeah.

DR. BELSITO: Okay. So discussion, respiratory boilerplate because it's in powders. Some evidence of eye irritation that's used at 7.5 percent and products that could be used about the eye. Negative sensitization at 20 percent. It's used up to 28 percent in a lipstick but we think that that's fine to clear that. Has low dermal penetration and a 28-day oral that's negative.

DR. SNYDER: Well, we have acute and 14-day, I don't think we have a 28-day.

DR. BELSITO: Oh, 14-day oral that's negative. But the low penetration gives us -- how to phrase this? Because of low penetration, we feel that we don't need the DART data? How would you -- come on wordsmith.

DR. SNYDER: Well, it was up to oral dose of 5 grams for 14 days.

DR. BELSITO: Right.

DR. SNYDER: Well, it just says no deaths, it doesn't say additional details. So, there was no toxicity signal in an ingredient that's not absorbed.

DR. BELSITO: Right. And the amount I had in a lipstick, the systemic exposure would be expected to be low given the amount and frequency of application.

DR. RETTIE: I mean a radiolabel study was done and had an actual number of less than 5 percent entering the skin.

DR. BELSITO: Right. So low dermal penetration gives us what? Not confidence but -- because of the low dermal penetration we do not think that additional chronic or an addition DART study -- or DART studies were needed.

DR. SNYDER: If you go to page 39 of the old original report, we did address from the 200--

DR. BELSITO: What's the pdf number, Paul?

DR. SNYDER: Thirty-nine. Page 39, on the right-hand column there. We addressed that few toxicity data were available for the Octyldodecyl Stearoyl Stearate.

DR. BELSITO: Right.

DR. SNYDER: And we included other safety assessments on how they're related. So, that was already included in our previous discussion.

DR. BELSITO: Right.

DR. SNYDER: So it's more than just --

DR. BELSITO: So we could bring that back into our discussions --

DR. SNYDER: I think so. As originally reported.

DR. BELSITO: -- that as originally reported, earlier safety assessments on Octyldodecyl Stearoyl Stearate were -- also helped to clear the tox and to support safety.

DR. SNYDER: And to support safety.

DR. BELSITO: And that would go in the discussion. Correct?

DR. SNYDER: Yes. So then it goes to re-review, not open?

DR. BELSITO: I don't know how we did this. We started the opening process.

MS. FIUME: Well, actually, you changed the conclusion. But it's going to be safe when formulated to be non-irritating.

DR. SNYDER: That's right. That's right. It was on 2001. No, but then went safe as used in 2005.

MS. FIUME: Right.

DR. BELSITO: Yeah, but now we have this irritation for the eye.

DR. SNYDER: Oh. Yeah, okay. Gotcha.

MS. FIUME: So, just for Regina's use, the paragraph that's in the previous discussion, can pretty much be used in the new discussion?

DR. SNYDER: I think so. I mean, you can just reference it and say as summarized in the summary of the 2005 report, other data were used to support safety.

DR. KLAASSEN: If you can hear me, I have a change in the summary on Page 19.

DR. BELSITO: Okay. So we have, again, the discussion, respiratory boilerplate that we have only a 14-day oral, but dermal penetration as low. And as noted in the original report, summary of data on Octyldodecyl Stearoyl Stearate were evaluated as a further basis for assessment of safety.

We noted that there was some eye irritation at 7.5 percent. And there is eye use in our conclusion. And that we have sensitization data up to 20 percent. We noted 28 percent in lipstick, but we thought this cleared it. And our conclusion was safe when formulated to be non-irritating. Am I missing anything?

MS. FIUME: Did you get that?

MS. TUCKER: Yes, I did.

DR. BELSITO: Great. Thanks, Regina.

DR. KLAASSEN: Hello?

MS. TUCKER: You're welcome.

DR. KLAASSEN: Hello?

DR. BELSITO: Curt, are you trying to say something? I can't hear you.

DR. KLAASSEN: On page 19, in our summary, in the third paragraph we have that 21.0112 percent Octyldodecyl Stearate was used. I would like to decrease that to four significant figures at the most and make that 21.01 percent. Even though the authors wrote it as six significant figures. And if we repeat that, that shows that we're equally as stupid as the authors.

So, there should not be more -- never more than four significant figures -- and that's exaggerating things in science if you use four significant figures. Using seven is -- I can't even think of a word that's so stupid.

DR. BELSITO: Okay. Well, let's hope the authors don't read the transcript. But Regina, drop it down to 21.01.

MS. TUCKER: Yes.

DR. KLAASSEN: And then that'll also be true in the results section too for that same number. It doesn't change the conclusion or anything.

DR. BELSITO: I'm glad I'm not the author. Whoa, scathing, Curt. Anything else? I may save this. Okay.

DR. KLAASSEN: I hope nobody in the room was an author.

DR. BELSITO: Hopefully not. But I'm going to contact them and have them read the minutes.

DR. KLAASSEN: Okay, please. And they can come contact me.

Cohen's Team – December 5, 2022

DR. COHEN: Octyldodecyl Stearoyl Stearate. Okay, so this has a history. In initial assessment, the panel found Octyldodecyl Stearoyl Stearate insufficient to determine safety in 2001. Subsequently, data needs were met, and a final amended report was published in 2005, which was safe for use. In September of 2022, the panel reopened the safety assessment because of updated usage data and significant increases in concentrations of use. So, we have 605 formulations, its use in lipsticks and max use went from 18 percent -- I'm sorry, 10 percent to 18 percent on the eye area. We have HRIPT at 21 percent in the original report. So, what are the comments from the group? Tom, you want to start?

DR. SLAGA: Yeah. Let me see. Well, as you stated, it was reviewed in 2005, and was safe. And this draft amended report now has some increase uses in concentrations and that's why we're opening. I still think that it's safe, though, to be honest. I don't see that that makes -- that there's sufficient change.

DR. COHEN: And we have higher concentrations around the eye. Susan, what was --

DR. TILTON: I mean, I noted overall the data there's dermal absorption, no in vitro or in vivo genotox, no oral acute toxicity, no or little ocular irritation. I noted that because of significant possibility of ingestion, high frequency use in lipsticks, highest concentrations could potentially include oral DART, but otherwise safe as used.

DR. ROSS: Yeah, I looked at this, I mean the tox, the LD50 looked very -- greater than 20 grams per kilo. The sub-chronic was very good. There was no DART, as Susan commented, however, there's genotox which was negative. Dermal was non-irritating up to 28 percent, if the definition of quote, "good dermatological tolerance" unquote is okay. I was going to ask my guru next door here with respect to whether that was going to be a reasonable interpretation. Sensitization is okay up to 21 percent in humans. The maximum use is 28 percent. With respect to the ocular, and remember we have an increased uses around the eye from 35 to 322. With respect to the ocular, we have a maximum use, at least in my notes, of 18.5 percent. The EYETEX in vitro assay, which is like a capsule-type assay I believe. That was tested up to 20.6 percent and that was okay. And there was some animal testing up to 12.7 percent with mixed results on irritation. So, when I looked at it with the whole thing, I didn't have too many concerns.

DR. COHEN: Yeah. That's how I had a safe as used. I think in the discussion we just bring up those changes on reopening. But the prior sensitization studies, we have ocular irritation studies were still valuable here and didn't change my final thoughts on this. But we have some new data in here and so we have a fresh report. And I think we could -- well, we're not presenting this one, but we'll see if they come out similarly to this.

DR. ROSS: Agreed.
DR. COHEN: Wilma, did you have anything?
DR. BERGFELD: No, I thought it was okay. I was just trying to see the status of it. So, we've reopened it, and now we're doing an amended report?
DR. HELDRETH: Right. We're at the draft amended report stage. So, if the panel, tomorrow, agrees that we can get to some sort of a safe conclusion, then it'll go out as a tentative amended report.
DR. COHEN: And what happens to it then?
DR. HELDRETH: So, a tentative amended report goes out and we give at least a 60-day comment period for anybody to respond to that new conclusion. And after that comment period is over, it'll come back to the panel at a future meeting. Unlikely to be at the very next meeting, but probably June or thereafter, as a draft final report. And that'll be potentially the last time the panel will look at it for a decade and a half.
DR. COHEN: It's been around for a while, this -- okay.
DR. HELDRETH: Now this was another one of the reports that had the two table formats. I didn't know if you wanted to comment.
DR. COHEN: Oh. Yes.
DR. BERGFELD: Is anyone changing their mind?
DR. COHEN: No. Those new tables are growing on me.
DR. BERGFELD: I thought you said yes to the new one.
DR. COHEN: No, I like the new one.
DR. BERGFELD: Susan and David said no.
DR. ROSS: Susan said the old one as well.
DR. BERGFELD: I thought both.
DR. HELDRETH: And then Tom could go either way.
DR. BERGFELD: I'd go for both.
DR. COHEN: Tom, what'd you like?
DR. SLAGA: Huh?
DR. COHEN: Which table you like?
DR. SLAGA: I can't hear you. Sorry.
DR. COHEN: Which table do you like? The old or the new?
DR. BERGFELD: Use table. Use table.
DR. COHEN: Use table, Tom. Sorry. That's very vague.
DR. SLAGA: The voice keeps shifting and I don't know why.
DR. COHEN: Can you hear me now? How about now, Tom?
DR. ROSS: You broke it.
DR. SLAGA: What was your final on the draft amended report for the oxy whatever?
DR. COHEN: Yeah. No, no, no. Yeah, this is for --
DR. BERGFELD: The use tables.
DR. COHEN: -- the Octyldodecyl Stearoyl Stearate. It was just, the question is which use table did you like better? The newer use table or the old use table?
DR. BERGFELD: Or both.
DR. SLAGA: Yeah, I think there's sufficient data to support it, too. Especially, irritation/sensitization and genotox.
DR. COHEN: Okay.
DR. SLAGA: This data with the higher levels.
DR. COHEN: Okay. So, if we're good to close that. And any comment on the use tables at all or no?
DR. SLAGA: No.
DR. COHEN: You like the new one or the old one?
DR. SLAGA: Well, in this case I liked the old one. It was quicker to read. But I can go either way, though. It doesn't matter to me.

DR. COHEN: All right.
DR. SLAGA: Whatever the majority is.
DR. COHEN: I think time will wear us all down and -- all right, so we're going to move on to Phytantriol.

Full Panel – December 6, 2022

DR. BELSITO: In 2005, we published a report that Octyldodecyl Stearate is safe for use in cosmetic products in the practices of use and concentration described in the safety assessment. And in September of 2022, we elected to reopen the safety assessment of the ingredient based upon updated usage data and significant increases in the concentration of use. I won't go through all of that data, but there were significant increases.
And, so we're looking at this again in light of the data we have and the reported increases including up to 28 percent in lip balms. We looked at all of the data. We did get sensitization at 20 percent; it's used up to 28, but we thought the 20 percent would cover it.
And, after looking at all the data, in light of the increased use in concentration, we still felt that it was safe as used when formulated to be nonirritating. And nonirritating was based upon some data that at 7.5 percent it caused eye irritation.
DR. COHEN: Seconded.
DR. BERGFELD: Seconded. And so this is going to go final?
DR. BELSITO: Um-hmm.
DR. BERGFELD: All those in favor of this conclusion of safe? Thank you, unanimous, again. Any further discussion to be added regarding the Stearate?
DR. BELSITO: No.
DR. BERGFELD: Okay. Moving on to the Zanthoxylum piperitum ingredients, Dr. Cohen.

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.

Amended Safety Assessment of Octyldodecyl Stearoyl Stearate as Used in Cosmetics

Status: Draft Final Amended Report for Panel Review
Release Date: February 10, 2023
Panel Meeting Date: March 6-7, 2023

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,

1620 L Street, NW, Suite 1200 ◊ Washington, DC 20036-4702 ◊ ph 202.331.0651
cirinfo@cir-safety.org

ABBREVIATIONS

CIR	Cosmetic Ingredient Review
Council	Personal Care Products Council
CPSC	Consumer Product Safety Commission
Da	daltons
DART	developmental and reproductive toxicity
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
wINCI; *Dictionary*	web-based *International Cosmetic Ingredient Dictionary and Handbook*

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of Octyldodecyl Stearoyl Stearate. Octyldodecyl Stearoyl Stearate is reported to function in cosmetics as a skin conditioning and viscosity increasing agent. The Panel reviewed the relevant new data concerning the safety of this ingredient in cosmetic formulations, as well as data from previously published safety assessments, and concluded that Octyldodecyl Stearoyl Stearate is safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating.

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., octyldodecanol, 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 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 octyldodecanol in 1985, with the conclusion that octyldodecanol 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.

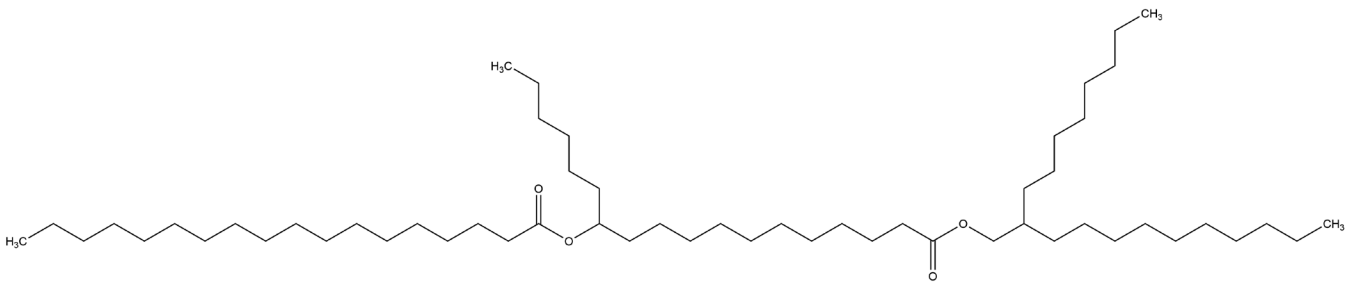


Figure 1. Octyldodecyl Stearoyl Stearate

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%.

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 this ingredient 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 this ingredient (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 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 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 found in the updated literature search, and unpublished data were not submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity (DART) 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 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. A clinical use study was performed using a lipstick containing 7.8% Octyldodecyl Stearoyl Stearate with 62 female subjects. The women applied the lipstick at least twice daily for 3 wk. No clinical changes were observed after use of the lipstick.*

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 21.01% 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 another 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.

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, 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. (The 2005 report should be consulted for additional studies that support the safety of Octyldodecyl Stearoyl Stearate.) 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 the previous assessment has been issued. In September 2022, the Panel determined that this safety assessment should be re-opened for re-evaluation due to a significant increase in concentrations 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 21.01% 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 DART or carcinogenicity studies on Octyldodecyl Stearoyl Stearate were found in an updated search of the published literature, and data were not submitted.

DISCUSSION

In 2005, the Panel published a final amended report with the conclusion that Octyldodecyl Stearoyl Stearate is 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 re-evaluates the conclusion of previously issued reports approximately every 15 years. At the September 2022 meeting the Panel re-opened the safety assessment of Octyldodecyl Stearoyl Stearate due to significant increases in concentration of use. (In 2022 the concentration of use in lipstick was 28%, compared to 10% in 2001.) Accordingly, the Panel reviewed all the new and existing data and concluded that Octyldodecyl Stearoyl Stearate is safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating.

As noted, this ingredient is now used at up to 28%. Concerns regarding dermal sensitization at this higher concentration of use were obviated by a negative HRIPT study of a formulation containing 21% Octyldodecyl Stearoyl Stearate. Accordingly, the Panel considered the lack of irritation and sensitization at this concentration sufficient to determine safety. However, the Panel was concerned that the potential exists for ocular irritation with the use of products formulated with Octyldodecyl Stearoyl Stearate. Accordingly, the Panel specified that products containing Octyldodecyl Stearoyl Stearate must be formulated to be non-irritating.

The Panel noted that DART and carcinogenicity data are absent. Nevertheless, because in vitro skin permeation and penetration data indicated absorption would be minimal and a 14-d oral toxicity study did not suggest this ingredient was systemically toxic, the need for DART studies was mitigated. Furthermore, the need for carcinogenicity data was mitigated by negative genotoxicity studies.

The Panel discussed the issue of incidental inhalation exposure resulting from this ingredient (for example, Octyldodecyl Stearoyl Stearate is reported to be used in face powders at concentrations up to 7.5%). Inhalation toxicity data were not available. However, the Panel noted that the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of this ingredient. Coupled with the small actual exposure in the breathing zone and the low concentrations at which this ingredient is used (or expected to be used) in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

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

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that Octyldodecyl Stearoyl Stearate is safe in cosmetics in the present practices of use and concentration described in this safety assessment when formulated to be non-irritating.

TABLES

Table 1. Updated and historical frequency (2022; 2001) and concentration (2020; 2001) of use according to duration and exposure

	# of Uses		*Max Conc of Use (%)*	
	Octyldodecyl Stearoyl Stearate			
	2022[7]	**2001[3]**	**2020[11]**	**2001[3]**
Totals	**605**	**106**	**0.50-28**	**2-15**
summarized by likely duration and exposure*				
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
as reported by product category				
Eye Makeup Preparations				
Eyebrow Pencil	2	2	0.75%	NR
Eyeliner	3	1	NR	4%
Eye Shadow	306	30	1.4-18.5%	4-10%
Other Eye Makeup Preparations	11	2	0.5-3.2%	NR
Fragrance Preparations				
Powders (dusting/talcum, excl aftershave talc)	NR	2	NR	4%
Other Fragrance Preparation	NR	1	NR	NR
Hair Preparations (non-coloring)				
Hair Conditioner	1	NR	NR	NR
Hair Coloring Preparations				
Hair Tints	NR	NR	3.3%	NR
Other Hair Coloring Preparation	NR	NR	3.5%	NR
Makeup Preparations				
Blushers (all types)	72	8	1.8-24%	2-7%
Face Powders	105	32	1.9-7.5%	2-7%
Foundations	12	5	0.5-6.7%	4-9%
Lipstick	48	1	3.4-28%	5-10%
Makeup Bases	2	5	6.1-24%	10%
Rouges	7	1	25.4%	NR
Other Makeup Preparations	18	1	1.9-3%	5%
Manicuring Preparations (Nail)				
Cuticle Softeners	NR	1	NR	NR
Nail Creams and Lotions	NR	1	NR	NR
Skin Care Preparations				
Cleansing	2	3	NR	NR
Face and Neck (exc shave)	NR	1	1% (not spray)	4%
Body and Hand (exc shave)	5	1	NR	15%
Moisturizing	7	4	2-9%(not spray)	NR
Night	NR	1	2.5% (not spray)	NR
Paste Masks (mud packs)	1	1	NR	NR
Skin Fresheners				
Other Skin Care Preparations	3	2	NR	NR
Suntan Preparations				
Suntan Gels, Creams, and Liquids	NR	NR	NR	8%

NR – not reported

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

**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

REFERNCES

1. Nikitakis J, Kowcz A. *International Cosmetic Ingredient Dictionary and Handbook*, Online Version (wINCI). http://webdictionary.personalcarecouncil.org/jsp/Home.jsp. 2022. Accessed: August 1, 2022.

2. Andersen FA (ed). Final report on the safety assessment of Octydodecyl Stearoyl Stearate. *Int J Toxicol*. 2001;20(Suppl 3):51-59.

3. Andersen FA (ed). Final amended report on the safety assessment of Octyldodecyl Stearoyl Stearate. *Int J Toxicol*. 2005;24(Suppl 3):65-74.

4. Burnett CL, Bergfeld WF, Belsito DV, et al. 2019. Final Report on the Safety Assessment of Fatty Acids & Fatty Acid Salts as Used in Cosmetics. Available from the Cosmetic Ingredient Review. (https://www.cir-safety.org/ingredients).

5. Andersen FA (ed). Annual Review of Cosmetic Ingredient Safety Assessments—2004/2005: Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol. *Int J Toxicol*. 2006;25(Suppl 2):73-78.

6. Fiume MM, Heldreth BA, Bergfeld WF, et al. Safety Assessment of Alkyl Esters as Used in Cosmetics. *Int J Toxdicol*. 2015;34(Suppl 2):5S-69S.

7. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2022. Voluntary Cosmetic Registration Program - Frequency of use of Cosmetic Ingredients. College Park, MD. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2022; received January 11, 2022.

8. European.Commission. CosIng database; following Cosmetic Regulation No. 1223/2009. http://ec.europa.eu/growth/tools-databases/cosing/. Last Updated 2020. Accessed October 5, 2022.

9. Anonymous. 2022. Use study summary of lip balms containing 28% Octyldodecyl Stearoyl Stearate. Unpublished data submitted by the Personal Care Products Council on September 29, 2022.

10. Anonymous. 2019. Repeated insult patch test on makeup base containing 21.0112% Octyldodecyl Stearoyl Stearate. Unpublished data submitted by the Personal Care Products Council on September 30, 2022.

11. Personal Care Products Council. 2020. Concentration of use by FDA Product Category: Octyldodecyl Stearoyl Stearate. Unpublished data submitted by the Personal Care Products Council on October 13, 2020.

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).

Received 15 May 2001; accepted 12 July 2001.

[1]Reviewed by the Cosmetic Ingredient Review Expert Panel. Rebecca S. Lanigan, former Scientific Analyst and Writer, prepared this report. Address correspondence to Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, USA.

International Journal of Toxicology, 20(Suppl. 3):51–59, 2001

1091-5818/01 $12.00 + .00

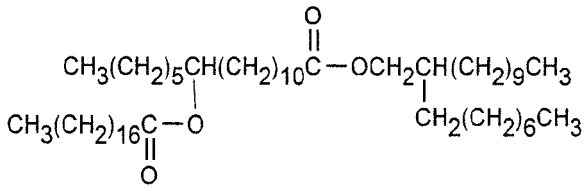


FIGURE 1
Octyldodecyl Stearoyl Stearate.

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).

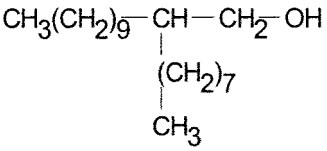


FIGURE 2
Octyl Dodecanol.

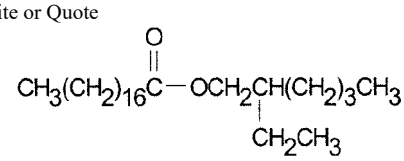


FIGURE 3
Octyl Stearate.

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.

REFERENCES

Alzo, Inc. 1998. Technical bulletin. Unpublished data submitted by CTFA, 11-23-98. (5 pages.)[2]

Consumer Product Testing. 1978. Primary dermal and ocular irritation (rabbits): Octyldodecyl Stearoyl Stearate. Unpublished data submitted by CTFA, 9-3-98. (11 pages.)[2]

Cosmetic, Toiletry, and Fragrance Association (CTFA). 1998a. Concentration of use. Unpublished data submitted by CTFA, 1-21-98. (2 pages.)[2]

CTFA. 1998b. Ocular irritation, primary and cumulative skin irritation, sensitization, and clinical in-use data. Unpublished data submitted by CTFA, 6-26-98. (27 pages.)[2]

CTFA. 1998c. Concentration of use data on Octyldodecyl Stearoyl Stearate. Unpublished data submitted by CTFA, 11-18-98. (1 page.)[2]

CTFA. 1999. Concentration of use data on Octyldodecyl Stearoyl Stearate. Unpublished data submitted by CTFA, 2/10/99. (2 pages.)[2]

Elder, R. L. 1985a. Final report on the safety assessment of stearyl alcohol, oleyl alcohol, and octyl dodecanol. *J. Am. Coll. Toxicol.* 4:1–29.

Elder, R. L. 1985b. Final report on the safety assessment of butyl stearate, cetyl stearate, isobutyl stearate, isocetyl stearate, isopropyl stearate, myristyl stearate, and octyl stearate. *J. Am. Coll. Toxicol.* 4:107–146.

Elder, R. L. 1987. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. *J. Am. Coll. Toxicol.* 6:321–401.

Food and Drug Administration (FDA). 1984. Concentration of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

FDA. 1998. Frequency of use of cosmetic ingredients. *FDA database*. Washington, DC: FDA.

Food and Drug Research Labs, Inc. 1983. Acute oral toxicity study in rats: Octyldodecyl Stearoyl Stearate. Unpublished data submitted by CTFA, 9-3-98. (12 pages.)[2]

Hill Top Research, Inc. 1983a. Report of a human skin test of cumulative irritation. Unpublished data submitted by CTFA, 6-26-98. (10 pages.)[2]

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

Hill Top Research, Inc. 1983b. Repeated insult patch test. Unpublished data submitted by CTFA, 6-26-98. (13 pages.)[2]

Japan Ministry of Health and Welfare. 2000. Pharmaceutical and Medical Safety Bureau Notification No. 990. Partial amendments to the enforcement regulations of the Pharmaceutical Affairs Law pertaining to the relaxation of regulations for cosmetics. September 29, 2000. Unofficial translation from Japanese.

International Specialty Products. 1998. MSDS. Unpublished data submitted to CTFA, 11-23-98. (3 pages.)[2]

ISP Van Dyke, Inc. 1997. Technical Information Sheet for Ceraphyl 847. Unpublished data submitted to CTFA, 9-3-98. (1 page.)[2]

Ivy Laboratories (KGL Inc.). 1991. Final report on the determination of the contact-sensitizing potential of concealer (07C) 97750-01 containing 5.0% octyldodecyl stearoyl stearate (RI1095) by means of the maximization test. Unpublished data submitted by CTFA, 6-26-98. (12 pages.)[2]

Santucci, L. G., ed. 1999. *List of Japanese cosmetic ingredients*, 4th ed., 83. Washington, DC: CTFA.

Sitek Research Laboratories. 1994a. In Vivo test for chemical induction of micronucleated polychromatic erythrocytes in mouse bone marrow cells. Unpublished data submitted by CTFA, 11-30-98. (52 pages.)[2]

Sitek Research Laboratories. 1994b. Evaluation of a test article in the *Salmonella typhimurium* plate incorporation mutation assay in the presence and absence of Aroclor-induced rat liver S-9 with a confirmatory study. Unpublished data submitted by CTFA, 11-30-98. (54 pages.)[2]

Trivent Chemical Company, Inc. 1998. Technical bulletin. Unpublished data submitted by CTFA, 11-23-98. (5 pages.)[2]

Wells Laboratories, Inc. 1993. Unpublished data submitted by CTFA, 11-23-98. (4 pages.)[2]

Wenninger, J. A., R. C. Canterbery, and G. N. McEwen, Jr., eds. 2000. *International Cosmetic Ingredient Dictionary and Handbook*, 8th ed., 921. Washington, DC: CTFA.

International Journal of Toxicology, 24(Suppl. 3):65–74, 2005

ISSN: 1091-5818 print / 1092-874X online
DOI: 10.1080/10915810500257113

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.

Received 15 April 2005; accepted 12 July 2005.
Address correspondence to F. Alan Andersen, Director, Cosmetic Ingredient Review, 1101 17th Street, NW, Suite 310, Washington, DC 20036, USA. E-mail: andersena@cir-saftey.com
[1]Reviewed by the Cosmetic Ingredient Review Expert Panel.

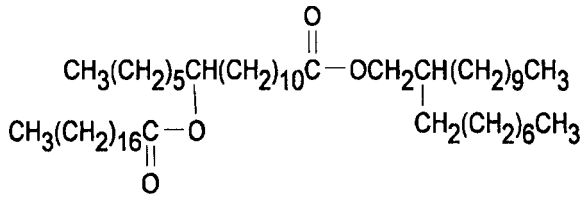


FIGURE 1
Octyldodecyl Stearoyl Stearate.

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).

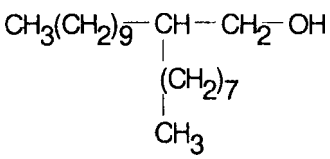


FIGURE 2
Octyl Dodecanol.

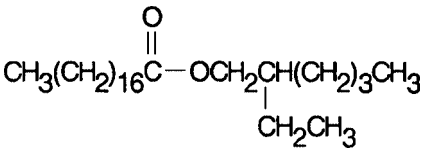


FIGURE 3
Octyl Stearate.

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.

REFERENCES

An-eX analytical services, Ltd. 2001. Human skin penetration and permeation of octyldodecyl stearoyl stearate from a simple vehicle—in vitro assessment. Unpublished data submitted by the Cosmetic, Toiletry, and Fragrance Association (CTFA). (18 pages.)[2]

Alzo, Inc. 1998. Technical Bulletin. Unpublished data submitted by CTFA, 11-23-98. (5 pages.)[2]

Consumer Product Testing. 1978. Primary dermal and ocular irritation (rabbits): Octyldodecyl Stearoyl Stearate. Unpublished data submitted by CTFA, 9-3-98. (11 pages.)[2]

Cosmetic Ingredient Reveiw (CIR). 1999. Final report on the safety assessment of Octyldodecyl Stearoyl Stearate.[3]

Cosmetic, Toiletry, and Fragrance Association (CTFA). 1998. Ocular irritation, primary and cumulative skin irritation, sensitization, and clinical in-use data. Unpublished data submitted by CTFA, 6-26-98. (27 pages.)[2]

CTFA. 2001. Current concentration of use data. Unpublished data submitted by CTFA. (1 page.)[2]

Elder, R L. 1985a. Final report on the safety assessment of stearyl alcohol, oleyl alcohol, and octyl dodecanol. *J. Am. Coll. Toxicol.* 4:1–29.

Elder, R L. 1985b. Final report on the safety assessment of butyl stearate, cetyl stearate, isobutyl stearate, isocetyl stearate, isopropyl stearate, myristyl stearate, and octyl stearate. *J. Am. Coll. Toxicol.* 4:107–146.

Elder, R L. 1987. Final report on the safety assessment of oleic acid, lauric acid, palmitic acid, myristic acid, and stearic acid. *J. Am. Coll. Toxicol.* 6:321–401.

European Commission (EC). 2002. Twenty-sixth Commission Directive 2002/34/EC of 15 April 2002 adapting to technical progress Annexes II, III, and VII to Council Directive 76/768/EEC. Brussels: EC.

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

Food and Drug Research Labs, Inc. 1983. Acute Oral Toxicity Study in Rats: Octyldodecyl Staroyl Stearate. Unpublished data submitted by CTFA, 9-3-98. (12 pages.)[2]

Hill Top Research, Inc. 1983a. Report of a human skin test of cumulative irritation. Unpublished data submitted by CTFA, 6-26-98. (10 pages.)[2]

Hill Top Research, Inc. 1983b. Repeated insult patch test. Unpublished data submitted by CTFA, 6-26-98. (13 pages.)[2]

International Specialty Products. 1998. Material Safety Data Sheet. Unpublished data submitted by CTFA, 11-23-98. (3 pages.)[2]

ISP Van Dyke, Inc. 1997. Technical Information Sheet for Ceraphyl 847. Unpublished data submitted to CTFA, 9-3-98. (1 page.)[2]

Ivy Laboratories (KGL Inc.). 1991. Final report on the determination of the contact-sensitizing potential of concealer (07C) 97750-01 containing 5.0% octyldodecyl stearoyl stearate (RI1095) by means of the maximization test. Unpublished data submitted by CTFA, 6-26-98. (12 pages.)[2]

Ministry of Health, Labor and Welfare (MHLW). 2001a. Unofficial translation of MHW Ordinance No. 331, Attached Table 1 [Negative List]. Ministry of Health Labor and Welfare, Pharmaceutical and Medical Safety Bureau, Inspection and Guidance Division, 2-2,1-chome, Kasumigaseki, Chiyoda-ku, Tokyo 100-8045, Japan.

MHLW. 2001b. Unofficial translation of MHW Ordinance No. 331, Attached Table 2 [Restricted List]. Ministry of Health Labor and Welfare, Pharmaceutical and Medical Safety Bureau, Inspection and Guidance Division, 2-2,1-chome, Kasumigaseki, Chiyoda-ku, Tokyo 100-8045, Japan.

MHLW. 2001c. Unofficial translation of MHW Ordinance No. 331, Appendix 4 [Ingredients of quasi-drugs] Ministry of Health Labor and Welfare, Pharmaceutical and Medical Safety Bureau, Inspection and Guidance Division, 2-2,1-chome, Kasumigaseki, Chiyoda-ku, Tokyo 100-8045, Japan.

Pepe, R. C., J. A. Wenninger, and G. N. McEwen, Jr., eds. 2002. *International cosmetic ingredient dictionary and handbook*. 9th ed., vol. 2. azl. Washington, DC: CTFA.

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

[3]Not available—superseded by this report.

Sitek Research Laboratories. 1994a. In vivo test for chemical induction of micronucleated polychromatic erythrocytes in mouse bone marrow cells. Unpublished data submitted by CTFA, 11-30-98. (52 pages.)[2]

Sitek Research Laboratories. 1994b. Evaluation of a test article in the *Salmonella typhimurium* plate incorporation mutation assay in the presence and absence of Aroclor-induced rat liver S-9 with a confirmatory study. Unpublished data submitted by CTFA, 11-30-98. (54 pages.)[2]

Trivent Chemical Company, Inc. 1998. Technical Bulletin. Unpublished data submitted by CTFA, 11-23-98. (5 pages.)[2]

Wells Laboratories, Inc. 1993. Unpublished data submitted by CTFA, 11-23-98. (4 pages.)[2]