Amended Safety Assessment of Cocoyl Hydrolyzed Collagen Ingredients as Used in Cosmetics

Status:	Draft Tentative Amended Report for Panel Review
Release Date:	May 16, 2025
Panel Meeting:	June 9-10, 2025

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.; Samuel M Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, 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., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Thushara Diyabalanage, Ph.D., Scientific Analyst/Writer, CIR.

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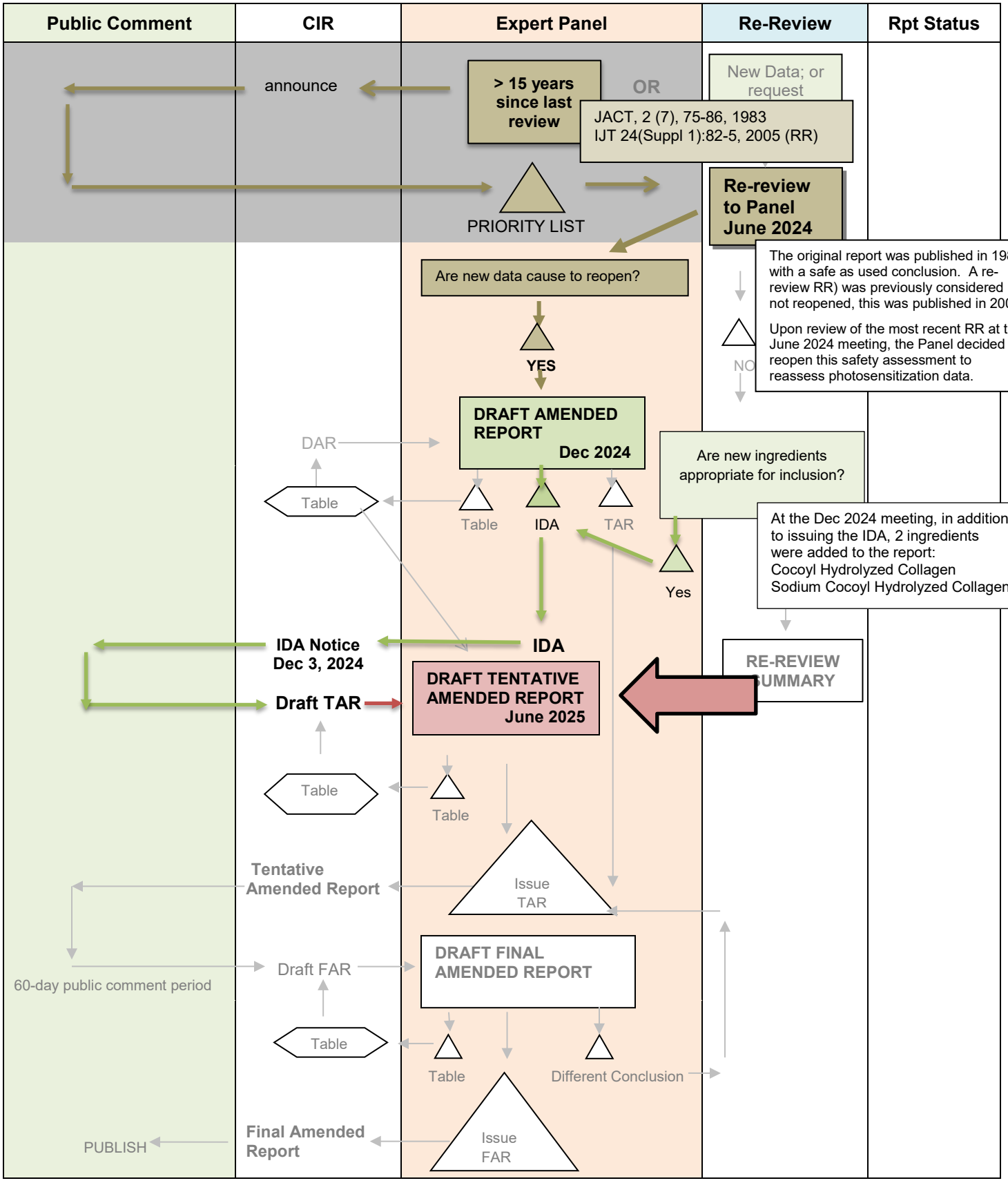
RE-REVIEW FLOW CHART

INGREDIENT/FAMILY Cocoyl Hydrolyzed Collagen Ingredients

MEETING June 2025



Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Thushara Diyabalanage, Ph.D., Scientific Analyst/Writer, CIR
Date: May 16, 2025
Subject: Tentative Amended Report of the Safety Assessment of Cocoyl Hydrolyzed Collagen Ingredients as Used in Cosmetics

The Expert Panel for Cosmetic Ingredient Safety (Panel) first published a Final Report on the Safety Assessment of Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein in 1983 (identified as *originalreport1983_HydrolyzedCollagens_062025* in the pdf). The Panel concluded that Potassium-Coco-Hydrolyzed Animal Protein and TEA-Coco-Hydrolyzed Animal Protein are safe as cosmetic ingredients in the present practices of use, as described in that report. The Panel previously considered a re-review of this report in 2002 and reaffirmed the 1983 conclusion, as published in 2005 (*rereview2005_HydrolyzedCollagens_062025*). Between the publication of the report in 1983 and the re-review, the names of these two ingredients as listed in the *International Cosmetic Ingredient Dictionary and Handbook* were subsequently changed to Potassium Cocoyl Hydrolyzed Collagen and Triethanolamine Cocoyl Hydrolyzed Collagen, respectively, and the latter is now named TEA-Cocoyl Hydrolyzed Collagen.

At the June 2024 meeting the Panel decided to reopen the safety assessment of Potassium and TEA-Cocoyl Hydrolyzed Collagen, concluding that some of the sensitization and photosensitization data included in the original report needed to be re-investigated. After reviewing the Draft Amended Report at the December 2024 meeting, the Panel decided to add 2 ingredients (Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen) to this safety assessment, and issued an Insufficient Data Announcement requesting the following information for all 4 ingredients:

- Maximum concentration of use
- Dermal irritation and sensitization data at a maximum concentration of use that does not induce sensitization.
- UV absorption spectra: if absorbed phototoxicity and/or photosensitization data.

The following data were received in response to the Insufficient Data Announcement. The new data information have been included in this report, as indicated by highlighted text. (A table is included at the end of this memo cross-referencing the data requested as compared to what was received.)

- Anonymous. 2007. Dermal irritation and sensitization of a product containing 3.2% Potassium Cocoyl Collagen. (*data1_HydrolyzedCollagens_062025*)
- Anonymous. 2022. Repeated insult patch test (liquid blush containing 0.1% Cocoyl Hydrolyzed Collagen). (*data2_HydrolyzedCollagens_062025*)
- Active Concepts. 2018. Dermal and ocular irritation tests AC Collagen Hydrolysate OS (Cocoyl Hydrolyzed Collagen). (*data3_HydrolyzedCollagens_062025*)
- Anonymous. 2001. Clinical safety evaluation repeated insult patch (emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen tested as received). (*data4_HydrolyzedCollagens_062025*)
- Anonymous. 2025. Summary information Potassium Cocoyl Hydrolyzed Collagen (irritation, sensitization, and UV absorption spectra) (*data5_HydrolyzedCollagens_062025*)
- Anonymous. 2025. "CIR Support" Potassium Cocoyl Hydrolyzed Collagen (irritation, sensitization, and photosensitization data) (*data6_HydrolyzedCollagens_062025*)
- Concentration of use by FDA Product category. 2025. (*data7_HydrolyzedCollagens_062025*)

In addition, the Council comments on the Draft Amended Report that were submitted prior to the December 2024 meeting and the responses to them are enclosed as well (*PCPCcomments_HydrolyzedCollagens_062025*; *response-PCPCcomments_HydrolyzedCollagens_062025*).

The following documents are included for your review.

- flow chart (*flow_HydrolyzedCollagens_062025*)
- report history (*history_HydrolyzedCollagens_062025*)
- search strategy (*search_HydrolyzedCollagens_062025*)
- data profile (*dataprofile_HydrolyzedCollagens_062025*)
- history *(history_HydrolyzedCollagens_062025)*
- transcripts from the meeting at which the current re-review was discussed (*trancripts_HydrolyzedCollagens_062025*)
- the minutes from all the previous meetings at which Potassium and TEA-Cocoyl Hydrolyzed Collagen was discussed during the original review and the rereview *(originalminutes_HydrolyzedCollagens_062025)*

The Panel should carefully consider and discuss the data (or lack thereof) and be prepared to issue a Tentative Amended Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion, and identify any additional items for inclusion in the Discussion.

IDA Data Needs:	Cocoyl Hydrolyzed Collagen	Potassium Cocoyl Hydrolyzed Collagen	Sodium Cocoyl Hydrolyzed Collagen	TEA-Cocoyl Hydrolyzed Collagen
Maximum concentration of use	N	Y	Y	N
Dermal irritation and sensitization data at max concentration of use that does not induce sensitization	Y	Y	N	N
UV absorption spectra: if absorbed phototoxicity and/or photosensitization data	N	Y	N	N

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: November 26, 2024

SUBJECT: Draft Amended Report: Safety Assessment of Potassium Cocoyl Hydrolyzed Collagen and TEA-Hydrolyzed Collagen as Used in Cosmetics (December 2-3, 2024 meeting draft)

The Personal Care Products Council respectfully submits the following comments on the Draft Amended Report, Safety Assessment of Potassium Cocoyl Hydrolyzed Collagen and TEA-Hydrolyzed Collagen as Used in Cosmetics.

Key Issue
Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen are also in the Dictionary. Should these two related ingredients be added to this report?

Additional Considerations
Cosmetic Use – It is misleading to call the VCRP data "ingredient-centric". The raw VCRP data are also "product-centric", it is just that FDA provided the VCRP data in a format that was "ingredient-centric". It is a difference in how the data were provided to CIR.

The Cosmetic Use section should also note that small businesses are exempt from reporting most product categories, and that a small business is defined as average gross annual sales of cosmetic products in the United States for the previous 3 years of <$1,000,000 adjusted for inflation and must not sell eye area products, injected products, internal use products, or products that alter appearance for more than 24 hours (see section 612).

Cosmetic Use – The new FDA cosmetic product categories split four makeup product categories (foundations, leg and body paints, makeup bases, other makeup preparations) into traditional or airbrush use, and asks about airbrush use of indoor tanning products, so some information on use in airbrush delivery systems may be available from the new FDA data. As part of the concentration of use survey, PCPC has also been asking for information on airbrush use, but so far, no such use has been reported. The airbrush information in the Cosmetic Use section needs to be revised to reflect these changes.

Cosmetic Use – In Europe, because it contains TEA, the TEA compound is limited to 2.5% in leave-on products. The following restrictions apply to the use of TEA in all products: Not to be used with nitrosating systems; Minimum purity: 99%; Maximum secondary amine content: 0.5% (applies to raw materials); Maximum nitrosamine content: 50 microg/kg; Keep in nitrite-free containers. The EU cosmetic regulations for TEA should be added to the cosmetic use section.

Sensitization, Human, old report summary – Please correct: "the test areaans a previously untreated site" (probably should be "the test area and a previously untreated site")

Summary – The use information from the new registration and listing data should be mentioned in the Summary.

Cocoyl Hydrolyzed Collagens - June 2025 – Thushara Diyabalanage Ph.D.	
Comment Submitter: Alexandra Kowcz, M.S., PCPC **Date of Submission: November 26, 2024**	
Comment	**Response/Action**
Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen are also in the Dictionary. Should these two related ingredients be added to this report?	Both these ingredients are added to this report
Cosmetic Use – It is misleading to call the VCRP data "ingredient-centric". The raw VCRP data are also "product-centric", it is just that FDA provided the VCRP data in a format that was "ingredient-centric". It is a difference in how the data were provided to CIR	Addressed
The Cosmetic Use section should also note that small businesses are exempt from reporting most product categories, and that a small business is defined as average gross annual sales of cosmetic products in the United States for the previous 3 years of	Addressed
Cosmetic Use – The new FDA cosmetic product categories split four makeup product categories (foundations, leg and body paints, makeup bases, other makeup preparations) into traditional or airbrush use, and asks about airbrush use of indoor tanning products, so some information on use in airbrush delivery systems may be available from the new FDA data. As part of the concentration of use survey, PCPC has also been asking for information on airbrush use, but so far, no such use has been reported. The airbrush information in the Cosmetic Use section needs to be revised to reflect these changes.	Addressed
Cosmetic Use – In Europe, because it contains TEA, the TEA compound is limited to 2.5% in leave-on products. The following restrictions apply to the use of TEA in all products: Not to be used with nitrosating systems; Minimum purity: 99%; Maximum secondary amine content: 0.5% (applies to raw materials); Maximum nitrosamine content: 50 microg/kg; Keep in nitrite-free containers. The EU cosmetic regulations for TEA should be added to the cosmetic use section	The Panel needs to review this recomendation
Sensitization, Human, old report summary – Please correct: "the test areaans a previously untreated site" (probably should be "the test area and a previously untreated site")	Addressed
Summary – The use information from the new registration and listing data should be mentioned in the Summary	Addressed

CIR History of:

Cocoyl Hydrolyzed Collagens

1983

First Safety Assessment- The Panel concluded that both Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagens were safe as used in cosmetics

2002

Re-reviewed, the Panel decided to not to re-open and re-affirmed their earlier conclusion, as published in 2005.

June 2024

Panel decided to reopen the safety assessment of these ingredients expecting to revisit some of the safety information related to sensitization and photosensitization.

December 2024

The Panel issued an insufficient data announcement (IDA). The IDA contained data needs for concentration of use, sensitization and UV absorption spectra (if absorbed, phototoxicity and photosensitization data) at maximum use concentrations.

The Panel also decided to add Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen to this safety assessment.

June 2025

The Panel considered a draft Tentative Amended Report Unpublished data that were received in response to the IDA have been added to the report.

Cocoyl Hydrolyzed Collagens - Data Profile* – June 2025 - Thushara Diybalanage

					Toxicokinetics			Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	Method of Mfg	Impurities	UV Absorption	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	Clinical Report	Case Reports
Cocoyl Hydrolyzed Collagen	X																			X					X					
Potassium Cocoyl Hydrolyzed Collagen	XO	**XO**	XO	X		O	O		O												XO	XO		XO	XO	XO		O	O	
Sodium Cocoyl Hydrolyzed Collagen	X																													
TEA-Cocoyl Hydrolyzed Collagen	XO	**O**	O						O												O	O		O	O	O		O		X

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

Cocoyl Hydrolyzed Collagens

Ingredient	CAS #	PubMed	FDA	HPVIS	NIOSH	NTIS	NTP	FEMA	EU	ECHA	ECETOC	SIDS	SCCS	AICIS	FAO	WHO	Web
Cocoyl Hydrolyzed Collagens	68952-15-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Sodium Cocoyl Hydrolyzed Collagens	68188-38-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Potassium Cocoyl Hydrolyzed Collagen	68920-65-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
TEA-Cocoyl Hydrolyzed Collagen	68952-16-9	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Search Strategy

PubMed

Search included key words 'Potassium Cocoyl Hydrolyzed Collagen', TEA-Cocoyl Hydrolyzed Collagen', Hydrolyzed Collagen Cocoyl and Sodium Cocoyl Hydrolyzed Collagens.

Search Engines Used

- Pubmed - http://www.ncbi.nlm.nih.gov/pubmed
  - appropriate qualifiers are used as necessary
  - search results are reviewed to identify relevant documents
- Connected Papers - https://www.connectedpapers.com/
- DeepDyve - https://www.deepdyve.com/

Pertinent Websites

- wINCI - https://incipedia.personalcarecouncil.org/winci/ingredient-custom-search/
- FDA Cosmetics page - https://www.fda.gov/cosmetics
- eCFR (Code of Federal Regulations) - https://www.ecfr.gov/
- FDA search databases: https://www.fda.gov/industry/fda-basics-industry/search-databases
- Substances Added to Food (formerly, EAFUS): https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus
- GRAS listing: https://www.fda.gov/food/food-ingredients-packaging/generally-recognized-safe-gras
- SCOGS database: https://www.fda.gov/food/generally-recognized-safe-gras/gras-substances-scogs-database
- Inventory of Food Contact Substances Listed in 21 CFR: https://www.cfsanappsexternal.fda.gov/scripts/fdcc/index.cfm?set=IndirectAdditives
- Drug Approvals and Database: https://www.fda.gov/drugs/development-approval-process-drugs/drug-approvals-and-databases
- FDA Orange Book: https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book
- OTC Monographs - https://dps.fda.gov/omuf
- Inactive Ingredients Approved For Drugs: https://www.accessdata.fda.gov/scripts/cder/iig/
- FEMA (Flavor & Extract Manufacturers Association) GRAS: https://www.femaflavor.org/fema-gras
- 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/
- EUR-Lex - https://eur-lex.europa.eu/homepage.html
- Scientific Committees (SCCS, etc) opinions: https://health.ec.europa.eu/scientific-committees_en https://health.ec.europa.eu/scientific-committees/scientific-committee-consumer-safety-sccs_en
- ECHA (European Chemicals Agency – REACH dossiers) – https://echa.europa.eu/
- 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
- EFSA (European Food Safety Authority) - https://www.efsa.europa.eu/en
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- AICIS (Australian Industrial Chemicals Introduction Scheme)- https://www.industrialchemicals.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- Office of Dietary Supplements https://ods.od.nih.gov/
- 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) IRIS library - https://apps.who.int/iris/
- a general Google and Google Scholar search should be performed for additional background information, to identify references that are available, and for other general information - www.google.com https://scholar.google.com/

JUNE 2024 PANEL MEETING – INITIAL REVIEW/RE-REVIEW

Belsito Team Meeting– June 3, 2024

DR. BELSITO: So, hydrolyzed animal protein and triethanolamine-coco-hydrolyzed animal protein in 1983 was reviewed. We concluded that they were safe as cosmetic ingredients in the present practice of use as described in the report. Since 1983, the names for the two ingredients have been changed. They are now potassium cocoyl hydrolyzed collagen and triethanolamine cocoyl hydrolyzed collagen, respectively. We reviewed these in 2002, reaffirmed the '83 conclusion.

So, it's been 15 years, and we're being asked to look at any new data, determine whether it needs to be reopened. An extensive scouring of the literature was done in April of 2024. No new relevant data were found in the literature.

Don't worry, Preethi, we moved on to a re-review.

And also is a current and historical use data. Basically, 2023 VCRP data, potassium cocoyl hydrolyzed collagen in two formulation, TEA-cocoyl hydrolyzed collagen, no reported uses. 2001, the ingredients were used in 64 and 20 formulations, respectively. Council survey in 2022, there were no concentrations of use reported. 2001, 20 percent non-coloring shampoo for the potassium cocoyl hydrolyzed, and TEA-cocoyl hydrolyzed, maximum of one percent in bubble baths. And so, that's our status.

The original report had sensitization at 10 percent and HR (inaudible) -- no other studies (inaudible). Okay.

So, my concern in not reopening it is that we will continue with the prior conclusion on this. And when I looked at the original report, there were reports of sensitization at 10 percent, and an HRIPT, and also positive photosensitization. There were no other studies to determine a non-sensitizing level. We have no concentration of use in this report, but prior uses of up to 20 percent in rinse-offs. I guess it's 0.2. I think I missed a decimal point. Or it's 0.02 in leave-ons. So, do we want to let that safety assessment sit out there?

I guess I wasn't on the Panel then, but I don't like having something, data, out there that says it photosensitizes and was a sensitizer at 10 percent; and it's being used in a bubble bath at 20 percent; and even though low concentration of leave-on, we don't a safe level of use in terms of sensitization, but photosensitizers are even of greater concern.

DR. EISENMANN: I wouldn't expect any data on these.

DR. BELSITO: I wouldn't either.

DR. EISENMANN: So, that's gonna be the problem.

DR. BELSITO: But then we would go insufficient rather than currently we say it's safe as used, based upon that old report. Right. If we don't reopen it, that's safe-as-use conclusion is out there with data giving percentages of how it was used in 2002. And I'm not sure that if I reviewed even the old data I would say that it's safe at those levels of use. I would want additional studies; in which case, it would go insufficient. Then per our ruling in two years, the conclusion would be whatever it is now. It's not --

DR. HELDRETH: Use not supported.

DR. BELSITO: Use not supported. Which I would prefer rather than having a document out there saying that this is safe as used, and we didn't reopen it when I looked at the old data and I wasn't so happy with the data that I saw, even though the use concentrations and the number of uses have declined.

DR. HELDRETH: Between now and when we would look at it again, we'll likely have Cosmetics Direct data. If that shows that there really are no reported uses at all, then when it was concluded, it would immediately go to insufficient data conclusion, zero use, as the conclusion instead of use not supported.

DR. BELSITO: Right. I think just for that reason -- again, looking at the old reports --

DR. SNYDER: Don, I support that motion to reopen and bring it up to date regarding the sensitization data.

DR. BELSITO: Yeah. And the photosensitization.

DR. SNYDER: Correct.

DR. BELSITO: Okay. Okay. So, now we can break for lunch. Allan, you have the report. You have the data that I need for the reports when my computer was down?

DR. RETTIE: Yes, I think we have --

DR. BELSITO: Can we meet now and do that? Shouldn't take long.

DR. RETTIE: Sure, assuming I have them. Maybe we need Curt as well. He'd been making notes.

DR. BELSITO: I thought you were writing it down. Curt took --

DR. KLAASSEN: Not me, but I'll listen.

DR. RETTIE: So, where we starting?

DR. KLAASSEN: I think it was -- Don, did you do the first two?

Cohen Team Meeting- [June 3, 2024]

DR. COHEN: Yeah. Potassium-coco-hydrolyzed animal protein and triethanolamine-coco-hydrolyzed animal protein. This was first published in 1983 with a safe as used conclusion. The names of the two ingredients have subsequently changed and now are potassium cocoyl hydrolyzed collagen and triethanolamine cocoyl hydrolyzed collagen respectively. The Panel considered re-review in 2002 and reaffirmed the 1983 conclusion.

It's been some time, over 15 years, so we're looking at it again. Based on the VCRP, potassium cocoyl hydrolyzed collagen is used in two formulations and the TEA cocoyl hydrolyzed collagen has no reported use. These had much more reported use in 2001. According to a council survey, no concentration of use were reported. In the past, it was used up to 20 percent in some shampoo and the TEA one percent in bubble bath.

The question to us is do we reopen? There didn't seem to be a lot of additional data to warrant a reopening.

DR. TILTON: I agree.

DR. ROSS: Agreed.

DR. COHEN: We're not going to reopen. As far as we can tell. Should we break before we go to the next one?

DR. BERGFELD: Yeah.

DR. ROSS: We can do the next one of these.

DR. COHEN: Okay.

Full Panel – June 4, 2024

DR. COHEN: Yes, so this group, Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein, was published in 1983 with a conclusion of safe as used in the present practice. The name on the two ingredients had subsequently changed to Potassium Cocoyl Hydrolyzed Collagen and Triethanolamine-Cocoyl Hydrolyzed Collagen respectively.

The Panel considered rereview in 2002 and reaffirmed the 1983 conclusion. The use of these ingredients has decreased substantially since the last review. And based on the data that we were presented, our motion was to not reopen.

DR. BERGFELD: Response?

DR. BELSITO: We didn't agree with that.

DR. BERGFELD: Okay.

DR. COHEN: Okay.

DR. BELSITO: If you look at the original report, there was sensitization at 10 percent and an HRIPT, and also a report of photosensitization. We had no information as to how to determine a non-sensitizing level for these. We have no concentration of use in this report, but the prior uses that would be referred to if we don't reopen it would be 20 percent in rinse-offs and I think 0.2 percent in leave-ons. I think we need to reopen it to reassess that photosensitization report. They report some sensitization at 10 percent. And, perhaps, again, with the new FDA reporting, get a sense of where these are being used. And if they are not being used, then we can accept the fact we have no concentration of use. If they are being used, then I think we need a concentration of use given the sensitization that was in the initial reports. I don't know how that got through, quite honestly.

DR. COHEN: Okay, so you want a re-adjudication of the conclusion from the last report, because it's not that long ago we have no concentration of use from the survey, right. So, you're hoping to get concentration of use from the survey, what if we don't have that?

DR. BELSITO: Well, then I think we have an issue with sensitization and photosensitization, don't we?

DR. COHEN: Okay, so, no reason not to amend my motion to reopen.

DR. BERGFELD: Is there a second to reopen?

DR. BELSITO: Second.

DR. BERGFELD: Any further discussion? Seeing none, call the question, all those in favor raise your hand, please.

DR. SNYDER: I agree.

DR. BERGFELD: Thank you. Thank you, Paul. Unanimous. And moving on to the last item is Dr. Belsito's group for MoS vs MoE.

DECEMBER 2024 MEETING – SECOND REVIEW/DRAFT AMENDED REPORT

Belsito Team Meeting – December 2, 2024

DR. BELSITO: Okay. So, when we left off, we were about to start cocoyl hydrolyzed collagen. And basically if you recall that this was up for a re-review because it had been more than 15 years since the last was published and there was a comprehensive literature search that was performed but the real reason for determining to reopen this was that in the original report there were some issues with sensitization and photosensitization that were not dealt with, I thought, at least adequately.

And so, we decided to reopen and take a look at that and also the new data that had come in. So, basically, I think that my take on this was that the data are insufficient, and we don't have a level below which sensitization is not seen. We also don't have a UV spectrum. Looking at the chemical formula I don't think it would absorb but I'll leave that to Allan, perhaps, to discuss. But I think if it does absorb in the A or the B range then we would need additional tests to rule out photosensitization and photo irritation. One of which could be like a ROS assay or other tests.

But that's where I was left with this ingredient that we don't have a level below which we don't have a clear NOAEL for sensitization and I'm not sure about this photosensitization data and it's used up to ten percent, is that correct?

DR. ZHU: Yes.

DR. BELSITO: Yeah. And sensitization and photosensitization were seen at ten percent, and I think the use may be higher than ten percent.

DR. EISENMANN: The current use, I got no concentration of use in 2022.

DR. BELSITO: Okay.

DR. EISENMANN: So that's the old use concentration.

DR. BELSITO: Okay. So then also insufficient for concentration of use. Paul, Curt, Allan?

DR. SNYDER: I agree.

DR. BELSITO: Okay, so we're going to go out with --

DR. RETTIE: I'm good.

DR. BELSITO: -- go ahead, Allan.

DR. KLAASSEN: Under method of manufacture, the last line, a fatty acid is neutralized with either Tea -- I think that should be capital E and capital A, I'd assume, rather than like coffee we want to have a tetraethylammonium.

DR. BELSITO: Where -- I'm sorry, Curt. I couldn't follow you.

DR. KLAASSEN: On methods of manufacture --

DR. BELSITO: What PDF?

DR. KLAASSEN: Last line --

DR. RETTIE: Twenty.

DR. KLAASSEN: -- it's -- what?

DR. RETTIE: PDF 20.

DR. KLAASSEN: Yeah, PDF page 20, methods of manufacture. It's just a small thing but we have tea, T-E-A, that should be a capital E or upper-case E, upper case A.

DR. BELSITO: Right.

DR. KLAASSEN: It should be tetraethylammonium and not --

DR. BELSITO: Yeah. Anything else?

DR. EISENMANN: In the dictionary cocoyl hydrolyzed collagen and sodium cocoyl hydrolyzed collagen are there and we have suppliers listed for all four ingredients so when I'm going out to suppliers I just feel I should do all four rather than just the two whether or not you decide -- because the data -- if somebody has data on the sodium it would support these other two, right?

DR. BELSITO: So, are we bringing these two into the report?

DR. EISENMANN: I don't know if you're going to bring them in or not, but I just feel like it makes sense to bring them in.

DR. BELSITO: Okay.

DR. EISENMANN: If you're going to spend a lot of time doing this report, doesn't it? I mean, that's my question. It's really a question.

DR. BELSITO: Yeah, I wasn't aware of the other two so what were the other two?

DR. EISENMANN: Well, cocoyl hydrolyzed collagen and sodium cocoyl hydrolyzed collagen. Which I don't have concentrations of use for but if I'm going to go out and ask for concentration of use on the two, I might as well add the other two to the survey.

DR. BELSITO: Sure. The more the merrier and there may be data on the other two that would support safety.

DR. EISENMANN: Right.

DR. BELSITO: Okay. So, we're going to add in cocoyl hydrolyzed collagen and sodium cocoyl hydrolyzed collagen to this. Allan, are you okay with that?

DR. RETTIE: I am.

DR. BELSITO: Curt, Paul?

DR. KLAASSEN: Yes.

DR. SNYDER: Yeah, I agree with that.

DR. BELSITO: Okay.

DR. SNYDER: Thank you, Carol for catching that.

DR. BELSITO: We're going to ask for concentration of use and also, we need a sensitization at concentration of use and UV spec and if it absorbs in the A or B range, other tests to evaluate photo irritation and photosensitization. Anything else? Okay, if not --

DR. RETTIE: Actually, one thing. We actually have a phototoxicity section in here. Good, but we don't seem to have --

DR. BELSITO: That's where this report got opened Allan. That was in the old report. That's not new data.

DR. RETTIE: Right. We have DART, genotox, and carcinogenicity tables but we have no sections in the report. Is that right? Yes.

DR. BELSITO: This is -- yeah. But those tables are summarizing old data. This is a report that we're reopening.

DR. RETTIE: Oh, yeah. Right, right, right. Got it.

DR. BELSITO: Anything else, Allan? Allan, anything else?

DR. RETTIE: Nothing.

DR. BELSITO: Okay.

Cohen Team Meeting – December 2, 2024

[**DR. COHEN:** Okay, Potassium Cocoyl Hydrolyzed animal protein and Triethanolamine Cocoyl Hydrolyzed animal protein. This was first published in 1983, with the conclusion that they were safe. The names of the ingredients had subsequently changed to what we're using now. The Panel considered a re-review of the report in 2002, and reaffirmed the 1983 conclusion as published in 2005, and it's been 15 years.

Based on the VCRP data, use has substantially decreased with the Potassium Cocoyl, and two formulations in the TEA Cocoyl Hydrolyzed Collagen having no reported uses. In 2001, reported concentration of use was 20 percent in a non-coloring shampoo and for TEA Cocoyl Hydrolyzed Collagen at 1 percent in a bubble bath. The RLD has 32 uses for Potassium Cocoyl Hydrolyzed Collagen and three for TEA Cocoyl Hydrolyzed Collagen.

In June, we reopened this because we wanted to reinvestigate sensitization and photosensitization data. So, this is before us today.

There is a description of the HRIPT at 10 percent for the Potassium Cocoyl Hydrolyzed Collagen and the TEA Cocoyl Hydrolyzed collagen with a few cases having some erythema and then ultimately a couple having some irritation. There was also a UVA study done here for photosensitization with UVA and UVB.

I'll open it up. The first comment was these are pretty large molecular weight products, aren't they? I mean they're mixtures, right, but aren't they pretty large molecular weight?

DR. ROSS: Yeah, I mean there should be -- I'm just looking at the dossier. Do we have that information?

DR. BERGFELD: It's 143.57.

DR. COHEN: Is that right with the collagen? When I looked it up outside I got much larger numbers.

DR. BERGFELD: It's in Table 1.

DR. TILTON: They are mixtures of different chain links, yes.

DR. COHEN: So having reopened this, does anyone have any comments about any data needs that they have?

DR. ROSS: Yeah.

DR. TILTON: We don't have current concentration of use.

DR. COHEN: Right, but --

DR. ROSS: I think we need -- as Susan said, we don't have concentrations of use. We need sensitivity data at the maximum concentration of use. We need photosensitivity data at maximum concentration of use. And I was a bit confused whether the current photosensitivity data was at a frequency of one of 28, or one of 19, or one of 9, which is how they subdivided the groups for the different UVA, UVB?

DR. COHEN: I'm not sure the dose of the light was.

DR. ROSS: Oh, is that right? Okay.

DR. COHEN: It seemed a little low considering like the summer sun can be 6 to 7 microwatts per centimeter squared. But I think under the test conditions it was Okay. What we're getting at here is that we have 10 percent HRIPT and we have 2001 concentration of use of 20 percent in a wash off product. But we don't have a lot of -- there's not much out there that these are problems.

And I thought the molecular weights would be larger. And by the way, what PDF was the molecular weight, again?

DR. BERGFELD: It's Table 1.

DR. ROSS: Yeah, I didn't see it in Table 1.

DR. BERGFELD: Chemical properties.

DR. COHEN: I'm looking at Table 1, it says definitions and reported functions on PDF 24.

DR. BERGFELD: I have it printed out.

DR. COHEN: Am I looking at the wrong thing?

DR. ROSS: I didn't see it there, so maybe I'm looking at the wrong thing.

DR. COHEN: Table 1 is PDF 24, Wilma? Is that what you're talking about?

DR. BERGFELD: I'm not looking at a PDF, I'm looking at print, so I don't have that.

DR. COHEN: Does your Table 1 say definitions and reported functions?

DR. BERGFELD: No, it says chemical properties.

DR. ROSS: If you go to method of manufacture section, there's some discussion there.

DR. COHEN: Okay.

DR. DIYABALANAGE: It's less than 600.

DR. ROSS: Yeah, well, if --

DR. BERGFELD: What did you say it was?

DR. ROSS: It's on PDF 20.

DR. DIYABALANAGE: It's permanently higher than 600.

DR. ROSS: So, yeah, they're pretty big.

DR. BERGFELD: I don't see that. I see under chemical properties on that same area 143.5- --.

DR. DIYABALANAGE: It's under method of manufacture.

DR. ROSS: Yeah, the middle of that method of manufacture paragraph.

MS. FIUME: Can a collagen weight vary?

DR. COHEN: Yeah, depending on the chain, right?

DR. ROSS: Yeah, a lot.

DR. DIYABALANAGE: They have different sizes.

MS. FIUME: Yeah.

DR. ROSS: And they're just talking about the polypeptide here, Thushara, to the fatty acid. No, they're not. Yeah. Nevertheless, to answer your question, they're big.

DR. COHEN: Yeah. Look, I think if this were a new report, I'd be coming at it a little harder. It's been around for a long time; we don't seem to see a lot of issues from them. We have a 10 percent concentration; the max use is on a wash off product. The max use for TEA Cocoyl Hydrolyzed Collagen is 1 percent and we have HRIPT at 10 times of that. I'm just wondering how hard I would of pushed this.

So, we need concentration of use which is old. But, Monice, aren't we going to hear that we got the survey and we didn't get it back, right? So we're not going to get that. And then we're going to say we want irritation and sensitization at a use from 20 some odd years ago, that was reaffirmed after the data that we already have seen.

DR. ROSS: Yeah, that was the concern when, I think, Don drove this, to reopen it. That the historical use was 20 percent and there were some reports of sensitization and photosensitization at 10 percent. So I don't think we need irritation. I think we need sensitivity and photosensitivity at maximum use.

DR. COHEN: Okay. Got it.

DR. BERGFELD: Can I interject? It has no uses now; it says it in the text.

DR. ROSS: Yeah.

DR. BERGFELD: Is that correct? At this point in time there's no use? And it's Annex 2 in Europe.

DR. COHEN: Well, we have uses from the RLD.

DR. DIYABALANAGE: RLD, yeah.

DR. BERGFELD: But the survey showed no uses?

DR. COHEN: Right, but I don't think we can any longer say there's no uses if the RLD is showing a use. Right?

DR. BERGFELD: Okay.

DR. COHEN: And the VCRP, in 2023, show 2 uses for Potassium Cocoyl Hydrolyzed Collagen.

MS. FIUME: David, as far as concentration of use, this was surveyed in 2022. And I don't think Carol is in this team and I don't know if Kim or Kathy can speak to it. I don't know if there are differences in response since the RLD information has become available, it could be higher or lower just because of everything they've had to do to submit to the FDA. So I don't know if something would be expected at this point that didn't come in two years ago as far as concentration of use because the survey is two years old.

DR. ROSS: Did someone say it was Annex 2? I must have missed that.

DR. BERGFELD: Yeah, I did.

DR. TILTON: Not this ingredient.

DR. ROSS: I don't think so, no.

DR. COHEN: I didn't know that.

DR. BERGFELD: I saw it here under uses, I think.

MS. FIUME: I don't think we have any European data for the hydrolyzed collagens.

DR. ROSS: Yeah, I'm not seeing it in here, but.

DR. COHEN: All right, look, we'll see how this is presented tomorrow. But it's been surveyed. We're using 23-year old concentration of use data, and the survey went out two years ago. We have sensitization at 10x the TEA Cocoyl Hydrolyzed Protein, and we have sensitization at half of max use on a wash off product. So we go out with the IDA and probably won't get anything, but we can try. But then we're faced with going out with the IDA having no data, and then what? Going out with an insufficient data conclusion?

DR. ROSS: Yeah.

DR. COHEN: Yes? Based on data that was adjudicated 20 some odd years ago as okay to use and very -- almost -- not zero, but very little data in the literature about this being a problem.

DR. ROSS: I agree there wasn't -- I didn't have too much of an issue with it.

DR. COHEN: I found three articles. By the way, I have three that'll be in my return that I don't think were listed in the report. Maybe they were, but I didn't see, maybe.

MS. FIUME: What wasn't listed, David?

DR. COHEN: A case report of allergic contact dermatitis to TEA Cocoyl Hydrolyzed Protein in the archives of Derm in 1976. Maybe it's there when I search. And that was by Emmett. There's a contact urticaria from protein hydrolysates in hair conditioners and an allergy in 1998. And hydrolyzed protein shampoo additives are not a common contact allergen, by Rycroft and McFadden, in contact dermatitis in 2000.

DR. ROSS: David, I guess the crux of this issue, if I can just ask you a quick question here, is the human HRIPT with 10 percent, we had a frequency of erythema of 5 out of 168. And the photosensitivity, it was 1/28. Or it could be 1/19 or one out of 9. But anyway, are those numbers problems?

DR. COHEN: Maybe we need to report -- maybe we need the raw data?

DR. ROSS: But my question is, would you see those as problems?

DR. COHEN: Yes, they certainly drew attention, but it said erythema no induration.

DR. ROSS: Okay.

DR. COHEN: Right. So I'm not sure if I read these as positive. And they were rechallenged. And during the rechallenge, 2 subjects produced allergic contact sensitization. So it went from 5 to 2, I don't know how that happens.

DR. ROSS: Yeah.

DR. COHEN: So, Okay. But the group looked at that and cleared it. Unless it was -- what we're saying, unless it was an error, right? But it's in the report. It's not an error in the report, right? It's not like a typo or something. It's in the report and the conclusion is made.

And then over the -- you know I haven't seen much in 24 years on this, but there was a little action on this, in '98 and '2000, indicating it's not a common sensitizer.

Okay. Look, we need concentration of use, sensitization of photo tox at max use. All right. I think we need to have another discussion about this.

DR. ROSS: Correct.

DR. TILTON: Yeah. You mentioned the fact that the 20 percent was in a rinse off. And I think the max concentration and leave on, the bubble baths was only 0.2 percent. That is much lower than the HRIPT, but it would be good to have current concentrations of use, certainly.

DR. COHEN: We all agree on the data needs. We've just been around the block a few times to fast forward and figure out how this is going to be figured through later on. Okay. There's nothing more to talk about on this. Can I go to Inositol?

DR. ROSS: Absolutely.

Full Panel – December 3, 2024

DR. BELSITO: Yeah. The Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen. We had looked at these in 1983 and concluded that they were safe as cosmetic ingredients in the present practice of use as described in the report. The names have been changed since that time. Then in 2002, we did a re-review and we reaffirmed the 1983 conclusion and that was published in 2005.

Because it was 15 years since the previous re-review was published it is up for re review at this time. A comprehensive literature search was conducted in April of 2024, and performed in October 2024, didn't find any new data. However, in June, we concluded that some of the sensitization and photosensitization data included in the original report needed to be reinvestigated and decided to reopen this.

And so, it has been reopened and I remain concerned about the sensitization and the photosensitization that's reported in this. I thought that this was insufficient for concentration of use, a use level below which sensitization is not seen, UV spectrum and if it absorbs in the A or B range, assays to assess for phototoxicity and photosensitization would be necessary.

And, Carol, I think you mentioned that there were two other ingredients that could be added to this report?

DR. EISENMANN: Yes, the dictionary includes Cocoyl Hydrolyzed Collagen itself and Sodium Cocoyl Hydrolyzed Collagen. And I looked at the suppliers and some of the suppliers have all four, so I feel comfortable going out to the suppliers and asking for data on all of them rather than just two.

DR. BELSITO: Right. So we would recommend that those two ingredients be added to this report.

DR. COHEN: So, Don, you had sensitization at max use was in your IDA?

DR. BELSITO: Yeah, concentration of use and then the use level below which sensitization is not seen. I mean, they could use sensitization at concentration of use or a negative sensitization study above that, I don't care. But they need to show me at what level they can use this product.

DR. COHEN: Okay. Second.

DR. BERGFELD: All right. So we had a second. Any other comments about this insufficient report? I'll call to question. All those opposed to this decision? Abstaining? It goes forward as an insufficient data announcement. Okay. Any comments about the editorials? Okay.

suggests the possibility that upon absorption BNPD may contribute to the endogenous formation of nitrosamines in man."

Dr. Beyer suggested writing a letter to Dr. Holland of Boots Co. Ltd. expressing the Panel's appreciation for his comments, and inviting him to submit the results of Boots' research on human skin absorption after the study is completed.

The Addendum to the Final Report on 2-Bromo-2-Nitropropane-1,3-Diol will shortly be announced as Final.

2. Hydrolyzed Animal Protein

The following conclusion of the report was unanimously approved:

"On the basis of the available animal and clinical data presented in this report, the Panel concludes that Hydrolyzed Animal Protein is safe as a cosmetic ingredient in the present practices of use and concentration."

Subject to minor revisions, the document will shortly be announced as a Tentative Report. Dr. McEwen said the CTFA adopted name for this ingredient has been changed to Hydrolyzed Collagen. Once this is confirmed in writing, the change will be incorporated into the report.

3. Stearyl Alcohol

The following conclusion of the report was unanimously approved:

"Based on the available data, Stearyl Alcohol, Oleyl Alcohol, and Octyl Dodecanol are safe as currently used in cosmetics."

Dr. Carlton suggested changing the title of section "Anti-Tumor Effect" to "Test for Anti-Tumor Effect." The group concurred. Dr. Carlton further stated the standard paragraph used in the Cosmetic Use section to qualify the

Amended Safety Assessment of Cocoyl Hydrolyzed Collagen Ingredients as Used in Cosmetics

Status: Draft Tentative Amended Report for Panel Review
Release Date: May 16, 2025
Panel Meeting: June 9-10, 2025

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.; Samuel M Cohen, M.D., Ph.D.; Curtis D. Klaassen, Ph.D.; Allan E. Rettie, Ph.D.; David Ross, 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., and the Senior Director is Monice Fiume, M.B.A. This safety assessment was prepared by Thushara Diyabalanage, Ph.D., Scientific Analyst/Writer, CIR.

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ABBREVIATIONS

Council	Personal Care Products Council
DBPS	disinfectant by-products
Dictionary	*International Cosmetic Ingredient Dictionary and Handbook*
FDA	Food and Drug Administration
FOU	frequency of use
HRIPT	human repeated-insult patch test
l.o.	leave-on
MoCRA	Modernization of Cosmetics Regulation Act
MTT	[3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NR	not reported
Panel	Expert Panel for Cosmetic Ingredient Safety
PII	primary irritation index
PUVA	Psoralen plus ultraviolet A
RLD	Registration and Listing Data
r.o.	rinse-off
SLS	sodium lauryl sulfate
TEA	triethanolamine
US	United States
UVA	ultraviolet A
UVB	ultraviolet B
VCRP	Voluntary Cosmetic Registration Program

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) reassessed the safety of Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen; two additional, structurally-similar, cosmetic ingredients (i.e., Cocoyl Hydrolyzed Collagen and Sodium Cocoyl Hydrolyzed Collagen) were added to this safety assessment. All 4 cocoyl hydrolyzed collagen ingredients are reported to function in cosmetics as hair conditioning agents, skin-conditioning agents, and surfactants. The Panel reviewed the available data to determine the safety of these ingredients. The Panel issued an amended report … [to be determined].

INTRODUCTION

This assessment reviews the safety of Cocoyl Hydrolyzed Collagen, Potassium Cocoyl Hydrolyzed Collagen, Sodium Cocoyl Hydrolyzed Collagen, and TEA-Cocoyl Hydrolyzed Collagen as used in cosmetic formulations. According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (*Dictionary*), these ingredients are reported to function in cosmetics as hair conditioning agents, skin conditioning agents, and surfactants - cleansing agents[1] (Table 1).

Two of the 4 ingredients named in this report have been reviewed previously. The Expert Panel for Cosmetic Ingredient Safety (Panel) published a review of the safety of Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen (then called Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein, respectively) in 1983.[2] The Panel concluded that these two ingredients are safe as cosmetic ingredients in the present practices of use, as described in that report. The Panel also considered a re-review of this report in 2002 and reaffirmed the 1983 conclusion, as published in 2005.[3] In accordance with its Procedures, the Panel evaluates the conclusions of previously issued reports every 15 years, and as it had been at least 15 years since the previous re-review was issued; accordingly, the Panel again considered a re-review of this ingredient at the June 2024 meeting. At that meeting, the Panel determined that this safety assessment should be re-opened to re-evaluate existing endpoints, particularly sensitization and photosensitization. Furthermore, at the December 2024 meeting, the Panel decided to include two structurally-related ingredients, i.e., Cocoyl Hydrolyzed Collagen and Sodium Hydrolyzed Collagen, in this safety assessment.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an extensive search of the world's literature; a search was last conducted in May 2025. 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 1983 report on Potassium and TEA-Coco-Hydrolyzed Animal Protein 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.) For complete and detailed information, the original 1987 report can be accessed on the CIR website (https://cir-reports.cir-safety.org/).

CHEMISTRY

Definition and Structure

The 4 ingredients named in this report are reviewed together in that they all are formed from the condensation of coconut acid chloride and hydrolyzed collagen.[1] Specifically, Cocoyl Hydrolyzed Collagen (CAS No. 68952-15-8) is the condensation product of coconut acid chloride and hydrolyzed collagen, while Potassium Cocoyl Hydrolyzed Collagen (CAS No. 68920-65-0), Sodium Cocoyl Hydrolyzed Collagen (CAS No. 68188-38-5), and TEA-Cocoyl Hydrolyzed Collagen (CAS No. 68952-16-9) are the potassium, sodium, and triethanolamine salts, respectively, of the condensation product (Table 1). The general formula for all these ingredients conforms to Figure 1.

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$$R\text{-}C(O)\text{-}NH\text{-}CHR'\text{-}C(O)\text{-}(NH\text{-}CHR''\text{-}C(O))_n\text{-}NH\text{-}CHR'\text{-}C(O)O^-Y^+$$

Figure 1. Cocoyl hydrolyzed collagen salt ingredients, wherein R-C(O)- represents the acyl moiety of the coconut acid; NH-CHR′-C(O)-(NH-CHR''-C(O))$_n$-NH-CHR′-C(O)O$^-$ represents the mixed peptides and polypeptides resulting from the hydrolysis of collagen; and Y$^+$ represents either the potassium, sodium, TEA cation and H (in the case of Cocoyl Hydrolyzed Collagen).[2]

Coconut acid is a mixture of fatty acids derived from *Cocos nucifera* (coconut) oil, varying in chain length from C6 to C18, but primarily comprising C12 (lauric acid ~44 - 52%), C14 (myristic acid ~13 – 19%), C16 (palmitic acid ~8 – 11%), and C10 (capric acid ~6 – 10%).[4] Coconut acid is first activated by conversion to the acid chloride, prior to amidation with peptides.[2] The hydrolysis of collagen can result in a random assortment of peptide or polypeptide chain lengths, and thus, "n" in Figure 1 may be as small as 2 or much greater.

Chemical Properties

Both Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen are slightly hazy amber liquids.[2] *Each ingredient has its own unique properties based on the size of the polypeptide and fatty acid moieties in the product.* According to a supplier, the average molecular weight of Potassium Cocoyl Hydrolyzed Collagen is around 600.[5]

Method of Manufacture

The source of collagen is chrome-leather splitting. This protein is hydrolyzed into short-chained polypeptides by acids, base or enzymes.[2] *The polypeptide chain fragments generated vary in length and molecular weight due to the random nature of this bond breaking process. At the next step, fatty acid chlorides (coconut fatty acids) are added so that an amide linkage is formed between the fatty acid chlorides and the free amino groups in the polypeptide. The polypeptide to the fatty acid ratios vary with the increasing molecular weight of the product. If the molecular weight is less than 600, the fatty acid moiety predominates, whereas when the molecular weight is higher than 600, the polypeptide predominates. At the final step of the production the fatty acid is neutralized with either TEA or potassium to form a salt.*

Potassium Cocoyl Hydrolyzed Collagen

According to a supplier, Potassium Cocoyl Hydrolyzed Collagen Product is prepared by condensation of coconut fatty acid and hydrolyzed collagen derived from fish scale.[5]

Composition/Impurities

Potassium Cocoyl Hydrolyzed Collagen

The impurities reported for Potassium Cocoyl Hydrolyzed Collagen (in order of predominance) include coconut fatty acid, hydrolyzed collagen, and inorganic salts such as sodium chloride, sodium sulfate, potassium chloride, and potassium sulfate.[2]

According to a supplier, Potassium Cocoyl Hydrolyzed Collagen is produced as a 30% solution in water.[5] The heavy metal content was reported as not more than 20 ppm and the content of arsenic was not more than 2 ppm. Another industry submission reported content of Potassium Cocoyl Hydrolyzed Collagen in a product is 20-40% in water.[6] The percentage of the dry substance was reported as 30-33%.

TEA-Cocoyl Hydrolyzed Collagen

The impurities reported for TEA-Cocoyl Hydrolyzed Collagen (in order of predominance) include coconut fatty acid, hydrolyzed collagen, triethanolamine sulfate, sodium chloride, and sodium sulfate.[2]

UV Absorption

Potassium Cocoyl Hydrolyzed Collagen

The ultraviolet (UV) absorption spectra was measured for Potassium Cocoyl Hydrolyzed Collagen (0.1% dilution in purified water).[5] The test material did not have a molar extinction coefficient > 1000 l/mol/cm at any wavelength between 290 - 700 nm.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of cocoyl hydrolyzed collagens in cosmetics. Data included herein were obtained from the FDA and in response to a survey of maximum use concentrations conducted by the Personal Care Products Council (Council), and it is these values that define the present practices of use and concentration. Frequencies of use obtained from the FDA include data from the Voluntary Cosmetic Registration Program (VCRP) database as well as Registration and Listing Data (RLD). As a result of the Modernization of Cosmetics Regulation Act (MoCRA) of 2022, the VCRP was discontinued in 2023 and, as of 2024, manufacturers and processors are required to register facilities and list their products (and ingredients therein) with the FDA (i.e., RLD). An exception is made for small businesses (average gross annual sales in the US of cosmetic products for the previous 3-yr period is less than $1,000,000, adjusted for inflation), which are exempt from MoCRA reporting for most cosmetic product categories. Eye area products, injected products, internal use products, or products that alter appearance for more than 24 h, and the facilities that manufacture these products, are not included in this exemption.[7] Please note, at this time, it is not appropriate to contrast data from the VCRP and RLD to determine a trend in frequency of use because there are numerous differences in the ways the data for the VCRP and the RLD were collected and processed, and because reporting frequency of use is now mandatory (as opposed to the past practice of voluntary reporting). Although the VCRP program is now defunct, trends in frequency of use from the RLD alone are not yet possible in that a baseline is currently not available.

According to RLD submitted in 2024, Cocoyl Hydrolyzed Collagen has the most reported uses, in 104 formulations[8] (Table 2; Table 3). However, the results of the maximum concentration of use survey collected by the Council in 2025 only reported use concentrations for Sodium Cocoyl Hydrolyzed Collagen (1.1% in other personal cleanliness rinse-off products)

and Potassium Cocoyl Hydrolyzed Collagen (0.01% in face and neck leave-on products).[9] Potassium Cocoyl Hydrolyzed Collagen is reported to be used in a product applied near the eye (an eye lotion; concentration of use not reported).

In comparing the number of uses reported in the VCRP in 2023 and 2001 for Potassium and TEA-Cocoyl Hydrolyzed Collagen, the frequency of use decreased for both ingredients.[3,10] Potassium Cocoyl Hydrolyzed Collagen was reported to have 64 uses in 2001 but only 2 in 2023; TEA-Cocoyl Hydrolyzed Collagen had 20 reported uses in 2001, but none in 2023.

Some products containing cocoyl hydrolyzed collagen ingredients may be marketed for use with airbrush delivery systems. With the advent of MoCRA and the current product categories outlined by the FDA, it is now mandatory that cosmetic products used in airbrush delivery systems be reported as such for some, but not all, product categories in the RLD. In other words, a reliable source of frequency of use data regarding the use of cosmetic ingredients in conjunction with airbrush delivery systems is now available, in some instances. Some of the reported product categories for these ingredients as listed in the RLD do require designation if airbrush application is used (e.g., foundations), but no airbrush use was indicated. Additionally, the Council currently surveys the cosmetic industry for maximum reported use concentrations of ingredients in products which may be used in conjunction with an airbrush delivery system; thus, this type of data may also be available, when submitted. Please note that no concentration of use data were provided indicating airbrush application. Nevertheless, 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. Without information regarding the consumer habits and practices data or product particle size data (or other relevant particle data, e.g., diameter) related to this use technology, the data profile is incomplete, and the Panel is not able to determine safety for use in airbrush formulations. Accordingly, the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

All of the cocoyl hydrolyzed collagen ingredients named in this report, except TEA-Cocoyl Hydrolyzed Collagen, are not restricted from use in any way under the rules governing cosmetic products in the European Union.[11,12] TEA-Cocoyl Hydrolyzed Collagen (as trialkylamines, trialkanolamines, and their salts) is listed in EU Annex III: List of Substances Which Cosmetic Products Must Not Contain Except Subject to the Restrictions. In leave-on products, the maximum concentration allowed is 2.5%. In both leave-on and rinse-off products, this ingredient is not to be used with nitrosating systems; must have a minimum purity of 99%; a maximum secondary amine content of 0.5% (applies to raw materials); a maximum nitrosamine content of 50 µg/kg; and is to be kept in nitrite-free containers.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Potassium Cocoyl Hydrolyzed Collagen

The oral LD_{50} of Potassium Cocoyl Hydrolyzed Collagen was 18.2 g/kg in rats.[2] In other studies, a single dose of 10 g/kg or up to 20 ml did not result in any deaths in rats.

TEA-Cocoyl Hydrolyzed Collagen

The oral LD_{50} of TEA-Hydrolyzed Collagen was 27.3 g/kg in rats.[2] In other studies, a single dose of up to 20 ml did not result in any deaths in rats.

Repeated-Dose Toxicity Studies

Repeated-dose toxicity studies on the cocoyl hydrolyzed collagen ingredients were not included in the original report, were not found in the updated literature search, and unpublished data were not submitted.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

Developmental and reproductive toxicity studies on the cocoyl hydrolyzed collagen ingredients were not included in the original report, were not found in the updated literature search, and unpublished data were not submitted.

GENOTOXICITY STUDIES

Genotoxicity studies on the cocoyl hydrolyzed collagen ingredients were not included in the original report, were not found in the updated literature search, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

Carcinogenicity studies on the cocoyl hydrolyzed collagen ingredients were not included in the original report, were not found in the updated literature search, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

The dermal irritation potential of Potassium and TEA-Cocoyl Hydrolyzed Collagen was evaluated in rabbits.[2] Potassium Cocoyl Hydrolyzed Collagen was non- to slightly irritating to rabbit skin at a concentration of 10%, and was mildly irritating when tested undiluted. TEA-Cocoyl Hydrolyzed Collagen was non-irritating to rabbit skin at a concentration of 10%, and was mildly/slightly irritating in 2 studies when tested undiluted, but was severely irritating in a

third study. In clinical studies, Potassium Cocoyl Hydrolyzed Collagen (2 and 20%; 24-h occlusive patches) was not an irritant in 33 subjects. Potassium and TEA-Cocoyl Hydrolyzed Collagen (24-h occlusive patch; 1.5 mg/cm^2) were not irritating in single-insult patch tests at 10%; of the 50 subjects tested, 29 were considered healthy and 8 had skin disease.

In guinea pigs, Potassium and TEA-Cocoyl Hydrolyzed Collagen were not sensitizers when tested at 10%. In a human repeated-insult patch test (HRIPT) in168 subject with 10% aq. Potassium and TEA-Cocoyl Hydrolyzed Collagen, 5 subjects challenged with Potassium Cocoyl Hydrolyzed Collagen were reported to have significant erythema, and were rechallenged at concentrations of 2.5, 5.0, and 10.0%. The results of both the initial challenge and subsequent rechallenge indicated that Potassium Cocoyl Hydrolyzed Collagen produced allergic contact sensitization in 2 subjects, cumulative irritation in 2 additional subjects, and a mild non-specific irritation in a fifth subject. The 2 subjects who were sensitized to Potassium Cocoyl Hydrolyzed Collagen were also sensitized to TEA-Cocoyl Hydrolyzed Collagen.

Details of the irritation, sensitization, and photosensitization studies summarized below can be found in Table 4.

Undiluted Cocoyl Hydrolyzed Collagen was predicted to be non-irritating in an EpiDerm™ dermal irritation test tissue viability was approximately 90%.[13] In rabbits, Potassium Cocoyl Hydrolyzed Collagen was non-irritating when tested as 10% active matter (24-h occlusive patch) and was a mild irritant when applied under occlusive patches for 4 or 24 h.[5,6] A 24-h occlusive patch of undiluted Potassium Cocoyl Hydrolyzed Collagen did not cause an irritation rection in 25 subjects.[5]

In a Buehler guinea pig test for sensitization, no contact hypersensitivity was observed with Potassium Cocoyl Hydrolyzed Collagen (30% active matter).[6] In human repeated-insult patch tests (HRIPTs), a formulation containing 0.1% Cocoyl Hydrolyzed Collagen (102 subjects),[14] an emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen (51 subjects),[15] and undiluted Potassium Cocoyl Hydrolyzed Collagen[5] did not product irritation or sensitization. Additionally, a formulation containing 3.2% Potassium Cocoyl Hydrolyzed Collagen (50 subjects) did not produce a significant cutaneous reaction in a primary and accumulated dermic irritation evaluation.[16]

Photosensitization

Potassium and TEA-Cocoyl Hydrolyzed Collagen, as 1% aq. solutions, did not result in UVB or UVA phototoxicity when the treated skin of 10 subjects was exposed to 7.5 J/cm^2 (15 min PUVA 6001). In a phototoxicity study with 28 subjects (randomly chosen from the 168 subjects that participated in the previously-described HRIPT), Potassium and TEA-Cocoyl Hydrolyzed Collagen was applied to the forearm, and 19 subject were irradiated with UVA only and 9 with UVA and UVB, One subject included in the photosensitization subgroup was sensitized to both Potassium and TEA-Cocoyl Hydrolyzed Collagen, and one additional subject was considered by the investigator to be photosensitized by both at the original challenge site at 72 h; only TEA-Cocoyl Hydrolyzed Collagen gave a similar value for this subject when challenged at a virgin site.

Potassium Cocoyl Hydrolyzed Collagen (9% active matter) did not produce a photosensitizing effect in Pirbright guinea pigs.[6] Study details were not provided.

OCULAR IRRITATION STUDIES

In Vitro

Cocoyl Hydrolyzed Collagen

An EpiOcular™ assay was performed to determine the ocular irritation potential of undiluted Cocoyl Hydrolyzed Collagen.[13] Deionized water was used as the negative control, and methyl acetate as the positive control. Tissue viability was approximately 85%; Cocoyl Hydrolyzed Collagen was considered to be non-irritating.

Animal

Potassium and TEA-Cocoyl Hydrolyzed Collagen

The ocular irritation of Potassium and TEA-Cocoyl Hydrolyzed Collagen was evaluated in rabbit eyes at concentrations of 10, 25, 50, and 100%.[2] In one study, both ingredients were minimally irritating at 10%, mildly irritating at 25 and 50%, and moderately irritating at 100%. In another study, concentrations of 10% were practically non-irritating to rabbit eyes, and the undiluted test material caused sever irritation,

CLINICAL STUDIES

A "large number" of healthy subjects and patients suffering from dermatitis used a 5% solution of a soap containing 41- 43% Potassium Cocoyl Hydrolyzed Collagen over a 10 – 48-d period.[2] Histological examinations of the treated area displayed a low irritation frequency, and no signs of sensitivity were observed.

Case Reports

Researchers stated there are occasional reports of contact urticaria to protein hydrolysate ingredients that are added to hair care products, soaps, bath gels, and creams.[17] Four different samples of commercial hydrolyzed proteins (5% aq.) from bovine collagen elastin and keratins (not identified) were sequentially patch-tested in 500 patients of the clinic; no positive reactions were noted. Additionally, 25 patients with scalp dermatitis to these allergens were prick-tested (0.1% aq.); again,

the results were negative. The researchers stated that although there was no evidence of hydrolyzed protein acting as a common contact allergen, it is recognized as being capable of producing reactions through a Type 1 mechanism.

In a clinical study was conducted to investigate the potential for the protein hydrolysates added to hair-care products to cause contact urticaria, 22 protein hydrolysates used in hair-care products (one of which was TEA-Cocoyl Hydrolyzed Collagen) were tested in scratch and patch tests in 11 hairdressers with hand dermatitis.[18] While some positive results were observed in the tests, none were seen with TEA-Cocoyl Hydrolyzed Collagen.

A 21-yr-old woman developed a severe dermatitis of the face after using a proprietary skin cleanser.[19] Patch testing showed delayed hypersensitivity to TEA-Cocoyl Hydrolyzed Collagen, but not to other ingredients of the cleanser. Further patch testing revealed positive results with other condensates of fatty acids and protein hydrolysates.

SUMMARY

The Panel published a safety assessment on Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen (then called Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein, respectively) in 1983 and concluded that these two ingredients are safe as cosmetic ingredients in the present practices of use, as described in that report. Subsequently, considered a re-review of these ingredients in 2002 and reaffirmed the 1983 conclusion, as published in 2005. In June 2024, since more than 15 years have passed since the last review, the Panel considered another re-review and determined to reopen the safety assessment to re-evaluate existing endpoints, particularly sensitization and photosensitization. Subsequently, the Panel decided to add two structurally-related ingredients, Cocoyl Hydrolyzed Collagen and Sodium Hydrolyzed Collagen, to this safety assessment.

According to 2024 RLD, Cocoyl Hydrolyzed Collagen has the most reported uses, in 104 formulations. However, the results of the maximum concentration of use survey collected by the Council in 2025 only reported use concentrations for Sodium Cocoyl Hydrolyzed Collagen (1.1% in other personal cleanliness rinse-off products) and Potassium Cocoyl Hydrolyzed Collagen (0.01% in face and neck leave-on products). TEA-Cocoyl Hydrolyzed Collagen (as trialkylamines, trialkanolamines, and their salts) is listed in EU Annex III: List of Substances Which Cosmetic Products Must Not Contain Except Subject to the Restrictions.

Undiluted Cocoyl Hydrolyzed Collagen was predicted to be non-irritating in an EpiDerm™ dermal irritation test tissue viability was approximately 90%. In rabbits, Potassium Cocoyl Hydrolyzed Collagen was non-irritating when tested as 10% active matter (24-h occlusive patch) and was a mild irritant when applied under occlusive patches for 4 or 24 h. A 24-h occlusive patch of undiluted Potassium Cocoyl Hydrolyzed Collagen did not cause an irritation rection in 25 subjects.

In a Buehler guinea pig test for sensitization, no contact hypersensitivity was observed with Potassium Cocoyl Hydrolyzed Collagen (30% active matter). In HRIPTs, a formulation containing 0.1% Cocoyl Hydrolyzed Collagen (102 subjects), an emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen (51 subjects), and undiluted Potassium Cocoyl Hydrolyzed Collagen did not produce irritation or sensitization. Additionally, a formulation containing 3.2% Potassium Cocoyl Hydrolyzed Collagen (50 subjects) did not produce a significant cutaneous reaction in a primary and accumulated dermic irritation evaluation. Potassium Cocoyl Hydrolyzed Collagen (9% active matter) did not produce a photosensitizing effect in Pirbright guinea pigs.

In an EpiOcular™ assay, undiluted Cocoyl Hydrolyzed Collagen was considered to be non-irritating. Tissue viability was approximately 85%.

Patch testing of commercial hydrolyzed proteins (5% aq.) from bovine collagen elastin and keratins in patients did not report positive results. In a study investigating the potential for the protein hydrolysates added to hair-care products to cause contact urticaria, a trade product containing TEA-Cocoyl Hydrolyzed Collagen did not produce positive results in scratch and patch tests in 11 hairdressers with hand dermatitis.

DRAFT DISCUSSION

[Note: This Discussion is in the draft form, and changes will be made following the Panel meeting.]

In accordance with its Procedures, the Panel re-evaluates the conclusion of previously-issued reports approximately every 15 years. The Panel published a safety assessment on Potassium Cocoyl Hydrolyzed Collagen and TEA-Cocoyl Hydrolyzed Collagen (then called Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein, respectively) in 1983 and concluded that these two ingredients are safe as cosmetic ingredients in the present practices of use, as described in that report. The Panel reaffirmed the 1983 conclusion, as published in 2005. Subsequently, at its June 2024 meeting, the Panel determined to reopen the safety assessment to re-evaluate existing endpoints, particularly sensitization and photosensitization, and subsequently decided to add two structurally-related ingredients, Cocoyl Hydrolyzed Collagen and Sodium Hydrolyzed Collagen, to this safety assessment. Therefore, this assessment reviews the safety of 4 cocoyl hydrolyzed collagen ingredients as used in cosmetic formulations, in accordance with the product categories and concentrations of use identified in the Use section and Use table. The Panel issued an amended report with the conclusion [TBD].

The Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings) notes that airbrush technology presents a potential safety concern. Although frequency and/or concentration of use data are now available (and in some cases mandated) for ingredients marketed for use with airbrush delivery systems in certain product categories, no data are available for consumer habits and practices thereof, product particle size, or other relevant particle data (e.g., diameter). As a result of deficiencies in these critical data needs, the data profile is incomplete, and the safety of cosmetic ingredients applied by airbrush delivery systems cannot be determined by the Panel. Accordingly, the Panel has concluded the data are insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

To be determined.

TABLES

Table 1. Definitions and reported functions[1]

Ingredient/CAS No	Definition	Reported Functions
Cocoyl Hydrolyzed Collagen (CAS No. 68952-15-8)	Cocoyl Hydrolyzed Collagen is the condensation product of coconut acid chloride and hydrolyzed collagen	hair conditioning agents skin-conditioning agents – misc. surfactants-cleansing agents
Potassium Cocoyl Hydrolyzed Collagen (CAS No. 68920-65-0)	Potassium Cocoyl Hydrolyzed Collagen is the potassium salt of the condensation product of coconut acid chloride and hydrolyzed collagen.	hair conditioning agents; skin-conditioning agents – misc; surfactants - cleansing agents
Sodium Cocoyl Hydrolyzed Collagen (CAS No. 68188-38-5)	Sodium Cocoyl Hydrolyzed Collagen is the sodium salt of the condensation product of coconut acid chloride and hydrolyzed collagen	hair conditioning agents skin-conditioning agents – misc surfactants-cleansing agents
TEA-Cocoyl Hydrolyzed Collagen (CAS No. 68952-16-9)	TEA-Cocoyl Hydrolyzed Collagen is the triethanolamine salt of the condensation product of coconut acid chloride and hydrolyzed collagen.	hair conditioning agents; skin-conditioning agents – misc; surfactants - cleansing agents

Table 2. Historical and updated frequency (RLD/VCRP) and concentration of use according to likely duration and exposure and by product category

	Potassium Cocoyl Hydrolyzed Collagen					TEA-Cocoyl Hydrolyzed Collagen				
	# of Uses			*Max Conc of Use*		*# of Uses*			*Max Conc of Use*	
	RLD (2024)[8]	**VCRP (2023)[10]**	**VCRP (2001)[3]**	**% (2025)[9]**	**% (2001)[3]**	**RLD (2024)[8]**	**VCRP (2023)[10]**	**VCRP (2001)[3]**	**% (2025)[9]**	**% (2001)[3]**
Totals*	**32**	**2**	**64**	**0.01**	**0.05-20**	**3**	**NR**	**20**	**NR**	**1**
summarized by likely duration and exposure**										
Duration of Use										
Leave-On	***	*1*	*4*	*0.01*	*0.05-0.2*	***	*NR*	*3*	*NR*	*NR*
Rinse-Off	***	*1*	*60*	*NR*	*1-20*	***	*NR*	*13*	*NR*	*NR*
Diluted for (Bath) Use	***	*NR*	*NR*	*NR*	*NR*	***	*NR*	*4*	*NR*	*1*
Exposure Type										
Eye Area	***	1	NR	NR	NR	***	NR	NR	NR	NR
Incidental Ingestion	***	NR	NR	NR	NR	***	NR	NR	NR	NR
Incidental Inhalation-Spray	***	NR	3[a]	NR	0.2[a]	***	NR	2	NR	NR
Incidental Inhalation-Powder	***	NR	NR	NR	NR	***	NR	NR	NR	NR
Dermal Contact	***	1	5	0.01	0.2	***	NR	12	NR	1
Deodorant (underarm)	***	NR	NR	NR	NR	***	NR	NR	NR	NR
Hair - Non-Coloring	***	1	29	NR	1-20	***	NR	8	NR	NR
Hair-Coloring	***	NR	30	NR	5	***	NR	NR	NR	NR
Nail	***	NR	NR	NR	0.05	***	NR	NR	NR	NR
Mucous Membrane	***	NR	NR	NR	NR	***	NR	5	NR	1
Baby Products	***	NR	NR	NR	NR	***	NR	1	NR	NR
as reported by product category										
Baby Products										
Baby Shampoos						NR	NR	1	NR	NR
Bath Preparations										
Bath Oils, Tablets, and Salts						NR	NR	1	NR	NR
Bubble Baths						NR	NR	3	NR	1
Eye Makeup Preparations (not children's)										
Eye Lotion	NR	1	NR	NR	NR					
Fragrance Preparations										
Perfumes						NR	NR	1	NR	NR
Hair Preparations (non-coloring)	***17***					***1***				
Hair Conditioners						NR	NR	1	NR	NR
Hair Sprays (aerosol fixatives)						NR	NR	1	NR	NR
Hair Straighteners	NR	NR	2	NR	NR					
Permanent Waves	12	NR	18	NR	1	NR	NR	2	NR	NR
Rinses (non-coloring)	2	NR	NR	NR	NR					
Shampoos (non-coloring)	1 (r.o.)	1	6	NR	1-20	NR	NR	3	NR	NR
Tonics, Dressings, and Other Hair Grooming Aids	2	NR	2	NR	NR					
Other Hair Preparations	NR	NR	1	NR	NR	1	NR	NR	NR	NR
Hair Coloring Preparations	***5***									
Hair Dyes and Colors (all types requiring caution statements and patch tests)	NR	NR	21	NR	5					
Hair Tints	NR	NR	9	NR	NR					
Hair Shampoos (coloring)	4 (r.o.)									
Other Hair Coloring Preparation	1 (l.o.)	NR	NR	NR	NR	1 (l.o.)	NR	NR	NR	NR
Makeup Preparations (not eye; not children's)										
Blushers and Rouges (all types)										
Foundations						NR	NR	1	NR	NR

Table 2. Historical and updated frequency (RLD/VCRP) and concentration of use according to likely duration and exposure and by product category

	Potassium Cocoyl Hydrolyzed Collagen					TEA-Cocoyl Hydrolyzed Collagen				
	# of Uses			*Max Conc of Use*		*# of Uses*			*Max Conc of Use*	
	RLD (2024)[8]	**VCRP (2023)[10]**	**VCRP (2001)[3]**	**% (2025)[9]**	**% (2001)[3]**	**RLD (2024)[8]**	**VCRP (2023)[10]**	**VCRP (2001)[3]**	**% (2025)[9]**	**% (2001)[3]**
Lipstick and Lip Glosses										
Makeup Bases										
Manicuring Preparations										
Nail Creams and Lotions	NR	NR	NR	NR	0.05					
Personal Cleanliness	***1***									
Other Personal Cleanliness Products	1 (r.o.)	NR	NR	NR	NR	NR	NR	1	NR	NR
Shaving Preparations										
Shaving Creams (aerosol, brushless, lather)						NR	NR	1	NR	NR
Other Shaving Preparation Products	NR	NR	1	NR	NR					
Skin Care Preparations	***9***					***2***				
Cleansing	NR	NR	3	NR	NR	NR	NR	4	NR	NR
Face and Neck (excluding shaving preparations)	9 (l.o.)	NR	NR	0.01	NR					
Body and Hand (excluding shaving preps)										
Moisturizing	NR	NR	1	NR	0.2	2	NR	NR	NR	NR
Other Skin Care Preparations										
Other Preparations (i.e., those preparations that do not fit another category)										

NR – not reported;
l.o. – leave-on; r.o. – rinse-off
*The total FOU provided for RLD refers to the ingredient count supplied by FDA, and is not a summation of the number of uses per category because each product may be categorized under multiple ***product*** categories. For data supplied via the VCRP or by the Council survey, the sum of all exposure types may not equal the sum of total uses because each ingredient may be used in cosmetics with multiple ***exposure*** types.
**Likely duration and exposure are derived from VCRP and survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
***Because RLD are product-centric and not ingredient-centric, each ingredient may be reported under several product categories, making a summation of RLD misleading in comparison to VCRP data. Accordingly, RLD are presented below by product category (as supplied by FDA), but are not summarized by likely duration and exposure.
[a] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.

Table 3. Frequency (RLD/VCRP) and concentration of use according to likely duration and exposure and by product category

	Cocoyl Hydrolyzed Collagen			Sodium Cocoyl Hydrolyzed Collagen		
	# of Uses		Max Conc of Use	# of Uses		Max Conc of Use
	RLD (2024)[8]	VCRP (2023)[10]	% (2025)[9]	RLD (2024)[8]	VCRP (2023)[10]	% (2025)[9]
Totals*	**104**	**2**	**NR**	**1**	**NR**	**1.1**
summarized by likely duration and exposure**						
Duration of Use						
Leave-On	***	*2*	*NR*	***	*NR*	*NR*
Rinse-Off	***	*NR*	*NR*	***	*NR*	*1.1*
Diluted for (Bath) Use	***	*NR*	*NR*	***	*NR*	*NR*
Exposure Type						
Eye Area	***	NR	NR	***	NR	NR
Incidental Ingestion	***	NR	NR	***	NR	NR
Incidental Inhalation-Spray	***	NR	NR	***	NR	NR
Incidental Inhalation-Powder	***	NR	NR	***	NR	NR
Dermal Contact	***	2	2	***	NR	1.1
Deodorant (underarm)	***	NR	NR	***	NR	NR
Hair - Non-Coloring	***	NR	NR	***	NR	NR
Hair-Coloring	***	NR	NR	***	NR	NR
Nail	***	NR	NR	***	NR	NR
Mucous Membrane	***	NR	NR	***	NR	NR
Baby Products	***	NR	NR	***	NR	NR
as reported by product category						
Bath Preparations	***1***					
Bath Oils, Tablets, and Salts	1	NR	NR			
Eye Makeup Preparations (not children's)						
Eye Lotion						
Hair Preparations (non-coloring)	***14***					
Hair Conditioners	2 (r.o)	NR	NR			
Permanent Waves						
Rinses (non-coloring)						
Shampoos (non-coloring)	4 (r.o)	NR	NR			
Tonics, Dressings, and Other Hair Grooming Aids						
Other Hair Preparations	4 (l.o): 4 (r.o)	NR	NR			
Hair Coloring Preparations						
Hair Shampoos (coloring)						
Other Hair Coloring Preparation						
Makeup Preparations (not eye or children's)	***42***					
Blushers and Rouges (all types)	11	NR	NR			
Lipstick and Lip Glosses	30	NR	NR			
Makeup Bases	1	NR	NR			
Personal Cleanliness				***1***		
Other Personal Cleanliness Products				1 (r.o)	NR	1.1
Skin Care Preparations	***46***					
Cleansing	9	NR	NR			
Face and Neck (excluding shaving preps)	14 (l.o); 10 (r.o)	2	NR			
Body and Hand (excluding shaving preps)	10 (l.o)	NR	NR			
Moisturizing	12	NR	NR			
Night	1	NR	NR			
Other Skin Care Preparations	8 (l.o)	NR	NR			
Other Preparations (i.e., those preparations that do not fit another category)	***1***					

NR – not reported; NA – not applicable (this category was not part of the VCRP)
l.o. – leave-on; r.o. – rinse-off
*The total FOU provided for RLD refers to the ingredient count supplied by FDA, and is not a summation of the number of uses per category because each product may be categorized under multiple ***product*** categories. For data supplied via the VCRP or by the Council survey, the sum of all exposure types may not equal the sum of total uses because each ingredient may be used in cosmetics with multiple ***exposure*** types.
**Likely duration and exposure are derived from VCRP and survey data based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)
*** In the RLD each ingredient may be reported under several product categories, making a summation of RLD misleading in comparison to VCRP data. Accordingly, RLD are presented below by product category (as supplied by FDA), but are not summarized by likely duration and exposure.
[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

Table 4. Dermal irritation and sensitization studies

Test Article	Vehicle	Concentration/Dose	Test Population/System	Protocol	Results	Reference
IRRITATION						
IN VITRO						
Cocoyl Hydrolyzed Collagen	none	undiluted	EpiDerm™ human epidermal model, developed with human epidermal keratinocytes	EpiDerm™ dermal irritation test DBPS was used as the negative control, SLS was the positive control	Nonirritating tissue viability was approximately 90% Controls gave expected results	13
ANIMAL						
Potassium Cocoyl Hydrolyzed Collagen	distilled water	10% active matter	6 New Zealand White rabbits	24-h occlusive patch (2.5 cm x 2.5 cm) on shaved abraded and non-abraded skin. Untreated control sites were shaved abraded and non-abraded skin	Non-irritating; PII = 0	6
Potassium Cocoyl Hydrolyzed Collagen	none	undiluted; 0.5 ml	3 male New Zealand White rabbits	4-h occlusive patch applied to clipped intact and abraded skin of the back (2.5 x 2.5 cm)	mild irritant; PII = 1.7 Very slight to well-defined erythema and very slight edema,	5
Potassium Cocoyl Hydrolyzed Collagen	none	0.5 ml, undiluted	6 New Zealand White rabbits,	24-h occlusive patch (2.5 cm x 2.5 cm) on shaved abraded and non-abraded skin. Untreated control sites were shaved abraded and non-abraded skin	mild irritant; PII = 1.59 Pronounced erythema on both test sites of all animals at 24 h after application; the effect was diminished but present in 5 animals at 72 h.	6
HUMAN						
Potassium Cocoyl Hydrolyzed Collagen	none	undiluted	25 female subjects	24-h occlusive patch test on the back of the subjects	No reaction at 30-60 min or 24 h after patch removal	5
SENSITIZATION						
ANIMAL						
Potassium Cocoyl Hydrolyzed Collagen (30% active matter)	distilled water	10%	Pirbright guinea pigs 10 treated, 5 control	Buehler method; test article was applied 1x/wk for 3 wk. Challenge was performed after 14 d (6-h patch)	No contact hypersensitivity was observed	6
HUMAN						
formulation containing 0.1% Cocoyl Hydrolyzed Collagen	none	neat	102 subjects	HRIPT; occlusive patches	Not an irritant or sensitizer	14
emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen	none	tested neat; 0.2 ml	51 subjects	HRIPT Induction consisted of 3, 24-h occlusive patches/wk for 3 wk Challenge was performed following a 2-wk non-treatment period	Not an irritant or sensitizer	15
formulation containing 3.2% Potassium Cocoyl Hydrolyzed Collagen,	NR	undiluted	50 subjects	Primary and accumulated dermic irritation evaluation.	No significant cutaneous reaction observed.	16
Potassium Cocoyl Hydrolyzed Collagen	Neat	undiluted; 0.2 ml	50 subjects	HRIPT Induction consisted of 3, 24-h occlusive patches/wk for 3 wk Challenge was performed following a 2-wk non-treatment period	Not an irritant or sensitizer	5
PHOTOSENSITIZATION						
ANIMAL						
Potassium Cocoyl Hydrolyzed Collagen (9% active matter)	not provided	not provided	Pirbright guinea pigs 10 males and 10 females/group	Details not provided	No photosensitizing effect	6

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JOURNAL OF THE AMERICAN COLLEGE OF TOXICOLOGY
Volume 2, Number 7, 1983
Mary Ann Liebert, Inc., Publishers

5

Final Report on the Safety Assessment of Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein

Potassium and TEA-Coco-Hydrolyzed Animal Proteins (PCHAP and TEA-CHAP) are salts of the condensation product of coconut acid and hydrolyzed animal protein. They are used in cosmetic products as detergents, foamers, and levelers.

Acute oral toxicity studies showed that both PCHAP and TEA-CHAP were practically nontoxic when ingested. Both ingredients at concentrations of 10%–100% were practically nonirritating to moderately irritating when instilled in the eyes of rabbits. Both were nonirritating to mildly irritating when applied at concentrations of 10%–50% to the skin of rabbits. Guinea pig sensitization studies with both PCHAP and TEA-CHAP were negative.

PCHAP and TEA-CHAP, at concentrations of 2%–10% were nonirritating to practically nonirritating in humans. In a repeated insult patch test, PCHAP gave a positive sensitization reaction in two of 168 subjects; two additional subjects showed cumulative irritation and one other was reported to have a nonspecific irritation. One subject out of 28 tested did not demonstrate significant irritation or sensitivity to either PCHAP or TEA-CHAP, but was photosensitized to both ingredients.

On the basis of the available information, the Panel concludes that Potassium-Coco-Hydrolyzed Animal Protein and TEA-Coco-Hydrolyzed Animal Protein are safe as cosmetic ingredients in the present practices of use as recorded in this report.

CHEMISTRY

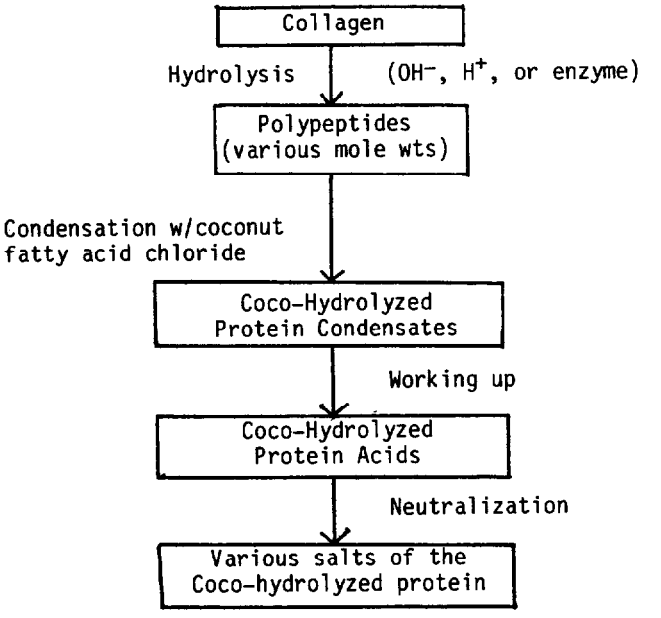
Structure

Potassium and Triethanolamine-Coco-Hydrolyzed Animal Proteins (PCHAP and TEA-CHAP, respectively) are salts of the condensation product of coconut acid and hydrolyzed animal protein. Each conforms to the structure:[1]

$$R\text{-}CO\text{-}NH\text{-}CHR'\text{-}CO\text{-}(NH\text{-}CHR\text{-}CO)_n\text{-}NH\text{-}CHR'\text{-}COO^-Y^+$$

where R-CO represents the acyl moiety of coconut fatty acid; R' represents the carbon chains of the mixed amino acids and polypeptides found in collagen (predominantly glycine, proline, alanine, and hydroxyproline); and Y^+ represents the potassium or TEA cation.

Chrome-leather splittings are used as a collagen source.[2] This protein material is hydrolyzed by acid, base, or enzymes into short-chained polypeptides. Due to random bond breaking during this step, polypeptide chains vary in length and molecular weight. Fatty acid chlorides (i.e., coconut fatty acid) are then added, forming amide linkages with the free amino groups on the polypeptide chain. The ratio of polypeptide to fatty acid changes with increasing molecular weight of the product. For molecular weights less than 600, fatty acids predominate, whereas at molecular weights greater than 600, the polypeptide predominates. In the final step of production, the terminal carboxyl group of the fatty acid is neutralized with either potassium or TEA ions to form a salt. The reaction temperature for preparing this ingredient varies between 60° and 100°C.[2] A typical manufacturing process of coco-hydrolyzed animal proteins is shown below.[3,4]



Properties

PCHAP and TEA-CHAP are clear to slightly hazy amber liquids. Table 1 lists some chemical and physical properties of these coco-hydrolyzed animal proteins. Each ingredient has unique properties which are dependent upon the proportions of polypeptide and fatty acid in the product.[4]

Viscosity of fatty acid hydrolyzed animal proteins is dependent on various conditions. Viscosity is high under conditions of low pH and low molecular weight (lower fatty acid content) and increases with time which may be a result of the orientation of the fatty acid.[4]

Coco-hydrolyzed animal proteins exhibit good foaming and detergent properties. As anionic tensides, their cleansing effect is dependent on low molecular weight and low pH conditions.[4]

These ingredients increase the skin and eye compatibility of anionic-active tensides (i.e., sodium laureth sulfate) without interfering with the cosmetic properties. The foaming and cleansing properties of sodium laureth sulfate were undisturbed by the addition of fatty acid hydrolyzed animal protein.[4]

Impurities and Additives

The impurities reported in PCHAP (in order of predominance) include: coconut fatty acid, hydrolyzed animal protein (collagen) and inorganic salts (sodium chloride, sodium sulfate, potassium chloride, and potassium sulfate).[1]

Impurities reported in TEA-CHAP (in order of predominance) include: coconut fatty acid, hydrolyzed animal protein (collagen), triethanolamine sulfate, sodium chloride, and sodium sulfate.[1] There were no reports of potential chemical interactions of either PCHAP or TEA-CHAP with other cosmetic ingredients. It is suspected that in the presence of nitrite and other nitrosating agents cosmetic preparations containing TEA-CHAP may give rise to N-nitrosodiethanolamine.

COSMETIC USE

Coco-hydrolyzed animal proteins are used in cosmetics as detergents, foamers, and levelers. In shampoos, the protective colloidal action of the

TABLE 1. Properties.

Property	*PCHAP*	*TEA-CHAP*
Solids (%)[a]	30%–38%	32%–40%
Ash (%)	7% maximum	0.8% maximum
Water (%)	70% maximum	60%–62%
pH	6.0–7.5	6.7–7.3
Possible additives	Ethylparaben, formaldehyde, sodium polyphosphate	Ethylparaben, formaldehyde, sodium polyphosphate

[a]Of the two suppliers of PCHAP and TEA-CHAP, the American manufacturer lists percent solids as 30%–38% and 32%–40%, respectively, while the German tab states that both ingredients contain 32% solids.

Data from Refs. 1,3.

polypeptide moiety prevents excessive defatting while the detergent activity produces good cleansing action.[3]

According to the industry's voluntary submissions to the Food and Drug Administration (FDA) in 1981, PCHAP is used in 251 cosmetic formulations. A concentration range of >25%–50% was reported for two shampoos and one skin

TABLE 2. Product Formulation Data.

Product category	Total no. of formulations in category	Total no. containing ingredient	No. product formulations within each concentration range (%)					
			>25–50	>10–25	>5–10	>1–5	>0.1–1	≤0.1
PCHAP								
Bubble baths	475	6	–	–	–	6	–	–
Other bath preparations	132	1	–	–	–	1	–	–
Hair conditioners	478	4	–	–	1	2	1	–
Hair straighteners	64	12	–	–	–	–	3	9
Permanent waves	474	55	–	–	–	6	48	1
Hair shampoos (noncoloring)	909	33	2	1	8	13	7	2
Tonics, dressings, and other hair grooming aids	290	6	–	–	–	2	3	1
Wave sets	180	1	–	–	–	1	–	–
Other hair preparations (noncoloring)	177	3	–	–	–	3	–	–
Hair dyes and colors (all types requiring caution statement and patch test)	811	43	–	–	5	38	–	–
Hair lighteners with color	2	1	–	–	–	1	–	–
Hair bleaches	111	1	–	–	–	1	–	–
Nail polish and enamel	767	74	–	–	–	–	–	74
Other manicuring preparations	50	6	–	–	–	3	–	3
Skin cleansing preparations (cold creams, lotions, liquids, and pads)	680	3	1	–	–	2	–	–
Face, body, and hand skin care preparations (excluding shaving preparations)	823	1	–	–	–	1	–	–
Other skin care preparations	349	1	–	–	–	–	1	–
1981 TOTALS		251	3	1	14	80	63	90
TEA-CHAP								
Hair conditioners	478	3	–	–	–	3	–	–
Hair shampoos (noncoloring)	909	11	1	–	1	1	7	1
Tonics, dressings, and other hair grooming aids	290	1	–	–	–	1	–	–
Cuticle softeners	32	1	–	–	–	–	–	1
Bath soaps and detergents	148	1	–	–	–	1	–	–
Other skin care preparations	349	1	–	–	–	1	–	–
1981 TOTALS		18	1	–	1	7	7	2

Data from Ref. 5.

cleansing cream. PCHAP is most commonly used in hair preparations. TEA-CHAP was reported in 18 formulations, usually in concentrations of up to 5%. Like PCHAP, it is generally found in hair preparations. A concentration range of >25%–50% was reported for one shampoo. Table 2 summarizes product formulation data for these two ingredients.[5]

The cosmetic product formulation computer printout which is made available by the FDA is compiled through voluntary filing of such data in accordance with Title 21 part 720.4 of the Code of Federal Regulations (1979). Ingredients are listed in prescribed concentration ranges under specific product type categories. Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the concentration in such a case would be a fraction of that reported to the FDA. The fact that data are submitted only within the framework of preset concentration ranges also provides the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a two- to 10-fold error in the assumed ingredient concentration.

Formulations which contain PCHAP or TEA-CHAP may come into contact with the face, hair and scalp, nails, axillae, and skin. These products are used daily or occasionally and their use may extend over years. Contact with formulations containing PCHAP or TEA-CHAP may last from seconds to several days.[5]

BIOLOGICAL PROPERTIES

General Effects

Collagen is often the protein used for hydrolysis in the preparation of these ingredients. This is partly because of its nonantigenic properties. Topical, intradermal, and subcutaneous sensitivity tests using collagen polypeptides (MW 110–1400) were performed on 50 male and 50 female guinea pigs. No antigenic responses or sensitivity resulted.[4]

Various ratios of sodium laureth sulfate to protein fatty acid condensates were tested for sucrase inhibition. Inhibition was nearly 100% for pure sodium laureth sulfate; however, when diluted to 60% or less with protein fatty acid condensate, there was no inhibition. Additionally, protein fatty acid condensates (at various molecular weights) were tested alone for sucrase inhibition. At molecular weights of 550 and 650, inhibition was negligible (3.5% and 0.5%, respectively) and nonexistent at molecular weights of 750, 900, and 1200.[4]

The adverse biological properties of protein fatty acid condensates include diminution of alkaline neutralization power of the skin, alteration of epidermal pH and eye irritation. Eye irritation appears to be inversely proportional to the molecular weight of the condensate and to the ratio of polypeptides in the product.[4]

Animal Toxicology

Acute Oral Toxicity

PCHAP and TEA-CHAP were tested for acute oral toxicity. Data are presented in Table 3. These studies indicate that PCHAP and TEA-CHAP are practically nontoxic when administered orally at the dosages specified.[6-8]

Acute Irritation

Ocular

Both PCHAP and TEA-CHAP were tested for rabbit eye irritation. Each ingredient was tested at 10%, 25%, 50%, and 100% concentrations. One-tenth ml of the test material at each dilution was instilled into one eye of six rabbits; the contralateral eye served as the control. Observations were made at 1, 2, and 8 h and each day for one week. Solutions containing 10% TEA-CHAP or PCHAP were reported to be minimally irritating with the most irritation (conjunctival only) subsiding by the second day of testing. Solutions containing 25% TEA-CHAP or PCHAP were defined as mildly irritating. Irritation disappeared after the second day. At a concentration of 50%, TEA-CHAP and PCHAP also caused mild irritation; however, irritation (corneal and conjunctival) lasted the duration of the experiment. Undiluted PCHAP and TEA-CHAP caused moderate irritation which also lasted the duration of the testing. Table 4 summarizes the results.[9-12]

In other studies, both PCHAP and TEA-CHAP were tested at concentrations of 10% and 100% for eye irritation. The Draize method was used as the test procedure, but an unknown method was used for scoring irritation. Each ingredient, at a concentration of 10%, caused minor conjunctival irritation which cleared by 72 h. The authors concluded that these materials were "practically nonirritating" at the concentration tested.[13,14] When the undiluted ingredient was instilled

TABLE 3. Acute Oral Toxicity of Coco-Hydrolyzed Animal Proteins.

Ingredient	*Dose (per kg)*	*No. of rats*	*Oral LD50 (per kg)*	*Ref.*
PCHAP	10.0 g	10	No deaths	6
PCHAP	10.4–29.5 g	20	18.2 g[a]	7
PCHAP	10 or 20 ml	10	No deaths	8
PCHAP	10 or 20 ml	10	No deaths	8
TEA-CHAP	15.89–44.9 g	20	27.3 g[b]	7
TEA-CHAP	10 or 20 ml	20	No deaths	8
TEA-CHAP	10 or 20 ml	20	No deaths	8

[a]Of the dead animals, the following observations were made: hyperemic lungs; "bleached" liver, kidneys and spleen; gastrointestinal tracts distended with sample; bloody nasal discharge; diuresis; hyperemic gastrointestinal tract and hardened sample in stomach. Of the survivors: five with red spotted lungs at dosage 10.4 ml/kg. Organs of the thorax and abdomen normal in others.

[b]Of the dead animals, the following observations were made: hyperemic lungs; "bleached liver and kidneys"; hyperemic gastrointestinal tract distended with sample; darkened spleen; hemorrhage of the gastrointestinal tract; bloody nasal discharge; diureseis and darkened liver.

TABLE 4. Eye Irritation.

Ingredient	*Concentration (%)*	*1 h*	*2 h*	*8 h*	*1 day*	*2 days*	*3 days*	*4 days*	*5 days*	*6 days*	*7 days*	*Area(s) affected*
PCHAP	10	7.33	9.33	9.33	3.00	0.67	0	0	0	0	0	Conjunctivae
PCHAP	10	6.33	8.00	5.67	0.67	0	0	0	0	0	0	Conjunctivae
PCHAP	25	12.00	14.33	10.67	2.33	0	0	0	0	0	0	Conjunctivae
PCHAP	25	17.33	18.67	16.00	10.67	0.67	0	0	0	0	0	Cornea and conjunctivae
PCHAP	50	11.33	14.33	14.67	4.83	4.33	1.17	0	0	0	0	Cornea and conjunctivae
PCHAP	50	15.33	15.67	15.00	14.50	7.50	1.33	0	0	0	0	Cornea and conjunctivae
PCHAP	100	10.33	13.33	11.33	8.83	3.33	0.33	0.33	0	0	0	Iris and conjunctivae
PCHAP	100	16.67	17.00	16.00	13.00	18.00	26.17	21.17	24.50	14.17	2.83	All
TEA-CHAP	10	7.33	8.33	6.67	2.00	1.00	0	0	0	0	0	Conjunctivae
TEA-CHAP	10	5.00	7.67	5.33	0	0	0	0	0	0	0	Conjunctivae
TEA-CHAP	25	12.67	14.33	13.00	6.00	0	0	0	0	0	0	Conjunctivae
TEA-CHAP	25	14.33	16.00	14.67	5.67	1.00	0	0	0	0	0	Conjunctivae
TEA-CHAP	50	10.67	13.00	12.00	1.67	0.33	0.33	0.33	0	0	0	Conjunctivae
TEA-CHAP	50	13.33	16.33	15.00	18.50	9.00	2.67	2.67	1.00	0.67	0.67	Cornea and conjunctivae
TEA-CHAP	100	13.67	17.00	29.50	12.50	5.33	3.33	3.00	3.00	2.17	1.50	Cornea and conjunctivae
TEA-CHAP	100	14.66	15.33	16.00	22.83	16.33	2.67	1.33	0.33	0.67	0	Cornea and conjunctivae

Based on the method of Draize (total possible score = 110).
Data from Refs. 9–12.

into eyes of rabbits, severe irritation developed in the cornea, iris, and/or conjunctiva. Irritation persisted throughout the 72 h observation period. These ingredients were considered to be eye irritants.[7,15]

Skin

Primary Irritation: PCHAP and TEA-CHAP were tested for potential skin irritancy in rabbits. The Draize method was used in all studies. PCHAP was reported to be nonirritating to slightly irritating when applied at a 10% concentration. Undiluted PCHAP was mildly irritating; erythema was the only skin response observed. At a concentration of 10%, TEA-CHAP was determined to be nonirritating to rabbits' skin. Undiluted TEA-CHAP was found to be slightly to mildly irritating in two studies; however, erythema, edema, and eschar formation were reported in one study which concluded that undiluted TEA-CHAP is severely irritating (PII = 3.05; maximum score = 8). Results of these tests are summarized in Table 5.[6-9,13]

Sensitization: PCHAP (0.1 ml of a 0.1% solution) was administered intracutaneously to the shaved skin of two white male guinea pigs. The injections were made every other day, three times weekly, until a total of 10 injections had been administered. Two weeks after the final induction injection, a challenge injection of 0.05 ml of the solution was made. Skin sites were scored 24 h following every injection and challenge scores were compared with induction scores. PCHAP elicited no responses to either induction or challenge injections and was considered to be nonsensitizing under the test conditions.[6]

Two samples each of PCHAP and TEA-CHAP at 10% were tested for potential sensitization according to the Buehler method. No reactions to test or challenge patches occurred in any of the guinea pigs (20 per ingredient). Both ingredients were considered to be nonsensitizing in all four tests at the given concentration.[9]

TABLE 5. Primary Skin Irritation.[a]

Ingredient	*No. of rabbits*	*Concentration (%)*	*PII*[b]	*Reactions*	*Comment*	*Ref.*
PCHAP	6	10	0.00	–	Nonirritating	8
PCHAP	6	10	0.50	erythema	Slightly irritating	8
PCHAP	6	100	1.59	erythema	Mildly irritating	9
PCHAP	6	100	1.26	erythema	Mildly irritating	9
PCHAP	6	100	1.04	erythema	Mildly irritating	6
PCHAP	6	100	1.88	eschar formation	Mildly irritating	7
TEA-CHAP	6	10	0.00	–	Nonirritating	8
TEA-CHAP	6	10	0.00	–	Nonirritating	8
TEA-CHAP	6	100	1.21	edema and erythema	Mildly irritating	9
TEA-CHAP	6	100	0.50	erythema	Slightly irritating	9
TEA-CHAP	6	100	3.05	eschar formation, edema, erythema	Severely irritating	7

[a]Method and scoring according to Draize.
[b]Primary Irritation Index (Maximum Score = 8).

CLINICAL ASSESSMENT OF SAFETY

Single Insult Patch Test

Patch tests were performed on 33 subjects using PCHAP at concentrations of 2% and 20%. Occlusive patches containing PCHAP at each concentration were applied to the chest or arm, and left in place for 24 h. Sites were scored upon patch removal and at 48 and 72 h. No reactions occurred.[16]

In another study, PCHAP and TEA-CHAP were simultaneously tested on 50 subjects. Two samples of each ingredient were tested at a concentration of 10%. Of the 50 subjects tested, at least eight had skin diseases (psoriasis and eczema) and many were being treated for illnesses (i.e., migraines, allergies, diabetes). There were 29 healthy subjects. Approximately 1.5 mg/cm^2 of each ingredient were applied under patches and left in place for 24 h. Sites were scored upon removal and at 48 and 72 h. One reaction (slight erythema at 24 h from a patch containing 10% PCHAP) occurred in a patient with psoriasis.[17] Table 6 summarizes the results of these studies.

Sensitization

A 5% solution of a soap containing 41%–43% PCHAP was used by a "large number of healthy subjects and people suffering from dermatitis" over a 10- to 48-day period. Histological examinations of the treated area indicated a low irritation frequency and no signs of sensitivity.[18]

A repeated insult patch test was performed on 168 subjects (115F, 53M) using 0.1 ml of a 10% water solution of PCHAP and TEA-CHAP. The test material was applied at 48 h intervals, three times per week for three weeks on the subjects' backs. The test area was occluded for 24 h, removed, and washed with distilled water. The test sites were read at 48 h, after which fresh test material and the occlusive patch were reapplied. After a three-week rest period, the test area, as well as a virgin site, were challenged using the same procedure as previously noted. The sites were scored for sensitization at 24, 48, and 72 hours. Five subjects challenged with PCHAP were reported to have significant erythema, and were rechallenged at concentrations of 2.5%, 5.0%, and 10.0%. The rechallenge was scored at 24, 48, and 72 h. The results of both the initial challenge and subsequent rechallenge indicated that PCHAP produced allergic contact sensitization in two subjects, cumulative irritation in two additional subjects, and a mild

TABLE 6. Single Insult Patch Test (Human).

Ingredient	*Concentration (%)*	*No. of subjects*	*Subject ages (yrs)*	*M/F*	*No. of reactions*	*Comments*	*Ref.*
PCHAP	2	33	20–76	18/15	0	nonirritating	16
PCHAP	20	33	20–76	18/15	0	nonirritating	16
PCHAP	10	50	15–59	22/28	0	nonirritating	17
PCHAP	10	50	15–59	22/28	1	1+ erythema at 24 h, 0 at 48 h	17
TEA-CHAP	10	50	15–59	22/28	0	nonirritating	17
TEA-CHAP	10	50	15–59	22/28	0	nonirritating	17

nonspecific irritation in a fifth subject. The two subjects who were sensitized to PCHAP were also sensitized to TEA-CHAP.[19]

Phototoxicity

One percent water solution of PCHAP and TEA-CHAP was tested on ten subjects under the regulations of the German Association for Light Research.[20] The investigator reported no UVB phototoxicity and no UVA phototoxicity when the treated skin was exposed to 7.5 J/cm^2 (15 min PUVA 6001).

Twenty-eight of the 168 subjects tested for irritation and sensitization discussed above were randomly selected to test the ability of PCHAP and TEA-CHAP to induce a phototoxic or photosensitive reaction following ultraviolet exposure. The test protocols were the same except that the forearm was used as a test site. The 28 subjects were divided into two groups; 19 received only UVA and 9 received both UVA and UVB. The UVA (320–400 nm) light was applied for 15 min to the 19 subjects (4.4 μW/cm^2 at the skin surface measured at a 360 nm wavelength peak). The UVB was applied at two times Mean Erythema Dose (MED) to nine subjects from a 150 watt Xenon Arc Solar Simulator emitting at 280–320 nm. The subjects receiving the UVB exposure were also exposed for 5 min to UVA as previously described. One subject included in the photosensitization subgroup reported above was sensitized to both PCHAP and TEA-CHAP. One additional subject who was considered by the investigator to be photosensitized by both PCHAP and TEA-CHAP at the original challenge site at 72 h. Only TEA-CHAP gave a similar value for this subject when challenged at a virgin site.[19]

Worker/Consumer Experiences

A chemical manufacturer has stated that he and his predecessor have produced protein derivatives for 40 years. During that time, there has been no case of sensitization or allergenic reaction by workers involved in the handling of these products.[21]

Approximately 600,000 units of a shampoo containing 1% TEA-CHAP have been sold without report of consumer complaint.[22]

SUMMARY

Potassium and TEA-Coco-Hydrolyzed Animal Proteins are salts of the condensation product of coconut acid and hydrolyzed animal protein. These two ingredients are prepared by the hydrolysis of collagen to short-chained polypeptides, then addition of coconut fatty acid and finally neutralization of the terminal carboxyl group of the fatty acid with either potassium or TEA. These ingredients have chemical and physical properties which are dependent upon their ratios of fatty acid to polypeptides. PCHAP is used in 251 and TEA-CHAP is used in 18 cosmetic products as detergents, foamers and levelers. Both ingredients are reported to be used primarily in rinse-off products, with one exception being a skin cleansing preparation.

Acute oral toxicity studies reveal that both PCHAP and TEA-CHAP are practically nontoxic when ingested. Both ingredients at concentrations of 10%–100% were practically nonirritating to moderately irritating when instilled in the eyes of rabbits. Both were nonirritating to mildly irritating when applied at concentrations of 10%–50% to the skin of rabbits. Guinea pig sensitization studies concluded that PCHAP and TEA-CHAP are nonsensitizing.

PCHAP and TEA-CHAP, at concentrations of 2%–10%, were nonirritating to practically nonirritating (one reaction in 50 subjects) when tested using a single insult patch test and a total of 266 patches.

In a repeated insult patch test PCHAP gave a positive sensitization reaction in two of 168 subjects; two additional subjects showed cumulative irritation and one other was reported to have a nonspecific irritation. The two subjects reported to be sensitized to PCHAP were also sensitized to TEA-CHAP. One subject out of 28 tested did not demonstrate significant irritation or sensitivity to either PCHAP or TEA-CHAP, but was photosensitized to both ingredients.

CONCLUSION

On the basis of the available information, the Panel concludes that Potassium-Coco-Hydrolyzed Animal Protein and TEA-Coco-Hydrolyzed Animal Protein are safe as cosmetic ingredients in the present practices of use as recorded in this report.

ACKNOWLEDGMENT

Mr. Kevin Fisher, Scientific Analyst and writer, prepared the technical analysis used by the Expert Panel in developing this report.

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[redacted]

POTASSIUM COCOYL HYDROLYZED COLLAGEN AND TRIETHANOLAMINE COCOYL HYDROLYZED COLLAGEN

A Safety Assessment of Potassium-Coco-Hydrolyzed Animal Protein and Triethanolamine-Coco-Hydrolyzed Animal Protein was published in 1983 (Elder 1983). Based on the data available at that time, the Panel concluded that these compounds were "safe as cosmetic ingredients in the present practices of use."

The names these two compounds as listed in the *International Cosmetic Ingredient Dictionary and Handbook* have been

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

changed to Potassium Cocoyl Hydrolyzed Collagen (CAS no. 68920-65-0) and Triethanolamine Cocoyl Hydrolyzed Collagen (CAS no. 68952-16-9), respectively (Pepe et al. 2002).

A search of the scientific literature databases to identify any new safety data relevant to the cosmetic use of Potassium Cocoyl Hydrolyzed Collagen and Triethanolamine Cocoyl Hydrolyzed Collagen yielded no new safety or toxicity data on either compound. The only new information related to these compounds is the updated frequency of use, as voluntarily reported by the industry to the FDA and shown in Table 22. The CIR Expert Panel considered these new uses and determined to not reopen this safety assessment.

Potassium-Coco-Hydrolyzed Animal Protein was used in 251 cosmetic products in 1981, with the highest concentration at 50% in non-coloring shampoos. In 2002, Potassium Cocoyl Hydrolyzed Collagen was used in 64 cosmetic products, with the highest concentration at 20% in noncoloring shampoo.

Triethanolamine-Coco-Hydrolyzed was used in 18 cosmetic products in 1981, with the highest concentration at 50% in noncoloring shampoos. In 2002, Triethanolamine Cocoyl Hydrolyzed Collagen was reported to FDA as used in 21 cosmetic products (FDA 2002), but an industry survey of current use concentrations did not provide any information (CTFA 2002).

The CIR Expert Panel acknowledged the new use of Triethanolamine Cocoyl Hydrolyzed Collagen in aerosol hair sprays. The effects of inhaled aerosols depend on the specific chemical species, the concentration, the duration of exposure, and site of deposition within the respiratory system. Particle size is the most important factor affecting the location of deposition (Jensen and O'Brien 1993). The mean aerodynamic diameter of pump hair spray particles is $\geq$80 μ, and the diameter of anhydrous hair spray particles is 60 to 80 μ. Typically less than 1% are below 10 μ, which is the upper limit for respirable particles (Bower 1999). Based on the particle size, Triethanolamine Cocoyl Hydrolyzed Collagen would not be respirable in formulation. Therefore, the Panel was not concerned about the lack of inhalation toxicity data.

The Panel also noted that the hydrolyzed protein would not absorb into human tissues, thus further reducing the risk of toxicity.

TABLE 22
Historic and current use of Potassium Cocoyl Hydrolyzed Collagen and Triethanolamine (TEA) Cocoyl Hydrolyzed Collagen

Product type	1976 uses (Elder 1983)	2001 uses (FDA 2001)	1976 use concentrations (Elder 1983) (%)	2001 uses concentrations (CTFA 2002) (%)
Potassium Cocoyl Hydrolyzed Collagen				
Bubble baths	6	—	>1–5	—
Bath preparations (other)	1	—	>1–5	—
Hair conditioners	4	—	>1–10	—
Hair straighteners	12	2	≤0.1–1	—
Permanent waves	55	18	≤0.1–5	1
Shampoos (noncoloring)	33	6	≤0.1–50	1–20
Hair tonics, dressings, etc.	6	2	≤0.1–5	—
Wave sets	1	—	>1–5	—
Hair preparations (other noncoloring)	3	1	>1–5	—
Hair dyes and colors	43	21	>1–10	5
Hair tints	—	9	—	—
Hair lighteners with color	1	—	>1–5	—
Hair bleaches	1	—	>1–5	—
Nail creams and lotions	—	—	—	0.05
Nail polish and enamel	74	—	≤0.1	—
Manicuring preparations (other)	6	—	≤0.1–5	—
Shaving preparations (other)	—	1	—	—
Skin cleansing creams, lotions, liquids, and pads	3	3	>1–50	—
Face and neck skin care preparations	1*	—	>1–5*	—
Body and hand skin care preparations		—		—
Moisturizers	—	1	—	0.2
Skin care preparations (other)	1	—	>0.1–1	—
Total uses/ranges for Potassium Cocoyl Hydrolyzed Collagen	**251**	**64**	**≤0.1–50**	**0.05–20**
Triethanolamine (TEA) Cocoyl Hydrolyzed Collagen				
Baby shampoos	—	1	—	—
Bath oils, tablets, and salts	—	1	—	—
Bubble Baths	—	3	—	1
Perfumes	—	1	—	—
Hair conditioners	3	1	>1–5	—
Hair sprays (aerosol fixatives)	—	1	—	—
Permanent waves	—	2	—	—
Shampoos (noncoloring)	11	3	≤0.1–50	—
Hair tonics, dressings, etc.	1	—	>1–5	—
Foundations	—	1	—	—
Cuticle softeners	1	—	≤0.1	—
Bath soaps and detergents	1	—	>1–5	—
Personal cleanliness products (other)	—	1	—	—
Shaving cream	—	1	—	—
Skin-cleansing creams, lotions, liquids, and pads	—	4	—	—
Skin care preparations (other)	1	—	>1–5	—
Total uses/ranges for Triethanolamine (TEA) Cocoyl Hydrolyzed Collagen	**18**	**20**	**0.1–50**	**—**

*This category was combined when the original safety assessment was performed and is now two separate categories.

As with all cosmetic ingredients derived from animal tissues, Potassium Cocoyl Hydrolyzed Collagen and Triethanolamine Cocoyl Hydrolyzed Collagen, as used in cosmetic products, must be free of detectable pathogenic viruses, prions, or other pathogenic agents.

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PROPYLENE GLYCOL STEARATE/PROPYLENE GLYCOL STEARATE SE

A Safety assessment of Propylene Glycol Stearate/Propylene Glycol Stearate Self-Emulsifying was published in 1983 (Elder 1983). Only one new study has been reported since then. This new study, along with the updated information below regarding types and concentrations of use, was considered by the CIR Expert Panel. After this review, the Panel determined that there was no need to reopen the safety assessment.

Data from the 1983 report on frequency of use and concentration of use (circa, 1976) is provided in Table 23, along with current frequency of use and total products in each category as provided by the FDA (FDA, 2002). An industry survey (CTFA 2002) uncovered no current concentrations of use of these ingredients.

In 1976, Propylene Glycol Stearate was used in 401 cosmetic preparations; currently Propylene Glycol Stearate is used in 193 cosmetic preparations. Eleven new product categories appeared in 2002.

Concentration of use in 1976 for Propylene Glycol Stearate ranged from 0.1% to 25%. In 1976, Propylene Glycol Stearate SE was reported in 131 cosmetic formulations; currently Propylene Glycol Stearate SE is used in 60 cosmetic formulations. Eight new product use categories appeared in 2002. Concentrations of use in 1976 for Propylene Glycol Stearate SE ranged from less than or equal to 0.1% to 25%.

REFERENCES

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SODIUM LAURETH SULFATE AND AMMONIUM LAURETH SULFATE

A Safety assessment of Sodium Laureth Sulfate and Ammonium Laureth Sulfate was published in 1982 (Elder 1982). New studies since then are listed at the end of this review. These new studies along with the updated information below regarding types and concentrations of use were considered by the CIR Expert Panel. After this review, the Panel determined that there was no need to reopen the safety assessment.

Data from the 1983 report on frequency of use and concentration of use (circa 1976) is provided in Table 24, along with current frequency of use and total products in each category as provided by the FDA (FDA 2002). Current concentration of use data from an industry survey are also provided (CTFA 2002).

In 1976, Sodium Laureth Sulfate was used in 282 cosmetic preparations, with the largest use in noncoloring shampoos at concentrations ranging from >1% to >50%. According to reports to FDA, Sodium Laureth Sulfate is reportedly now used in 952 cosmetic preparations (FDA 2002), with the largest use in shampoos at 11% to 50% (CTFA 2002). This ingredient is used in 23 product categories in 2002 that were not in the 1976 FDA data.

In 1976, Ammonium Laureth Sulfate was used in 63 cosmetic preparations, with the largest use in hair dyes and colors at >5% to 25%. Currently Ammonium Laureth Sulfate is used in 244 cosmetic preparations, with the largest use in shampoos at >0.1% to >50%. This ingredient was used in 11 product categories in 2002 that were not in the 1976 FDA data.

The Panel reiterated that the previously existing and the new data demonstrate the irritancy of Sodium Laureth Sulfate and Ammonium Laureth Sulfate in leave on products. The available data do suggest that these ingredients are toxic in animal tests via inhalation exposure and they are used in products that may be aerosolized.

The effects of inhaled aerosols in humans depend on the specific chemical species, the concentration, the duration of

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

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

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: November 20, 2024

SUBJECT: Potassium Cocoyl Hydrolyzed Collagen

Anonymous. 2007. Dermal irritation and sensitization of a product containing 3.2% Potassium Cocoyl Hydrolyzed Collagen.

RESULTS

55 volunteers were invited and 53 were selected for accomplishment of this study. These, 01 was excluded during the phase of Dermic Irritation Accumulated by presenting description of atopia unrelated in the inclusion of the study.
02 volunteers didn't return for the final evaluation for personal reasons unrelated to the study.

PRIMARY DERMIC IRRITATION AND ACCUMULATED DERMIC IRRITATION

None of the 52 volunteers has presented significant cutaneous reaction after the study period. See table 1.

SENSITIZATION

None of the 50 volunteers has presented significant cutaneous reaction after the study period. See table 2.

Table 1: Results obtained during the primary and Accumulated Dermic Irritation evaluation in 52 volunteers.

Evaluation Days of the Areas in the Back after Patches Application Following the ICDRG Scale																				
Nº. Vol.	**Primary Dermic Irritation**				**Accumulated Dermic Irritation**															
	3rd		5th		3rd		5th		8th		10th		12th		15th		17th		19th	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
01	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
02	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
03	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
04	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
05	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
06	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
07	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
08	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
09	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
11	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
13	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
17	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
18	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
19	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
20	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Evaluation Days of the Areas in the Back after Patches Application Following the ICDRG Scale																				
Nº. Vol.	**Primary Dermic Irritation**				**Accumulated Dermic Irritation**															
	3rd		5th		3rd		5th		8th		10th		12th		15th		17th		19th	
	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B
21	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
22	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
23	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
24	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
25	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
26	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
27	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
28	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
29	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
30	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
31	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
32	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
33	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
34	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
36	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
37	-	-	-	-	-	-	-	-	Excluded											
38	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
39	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
40	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
41	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
42	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
43	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
44	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
45	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
46	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
47	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
48	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
49	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
51																				
52																				
53																				
54	Didn't selected																			
55	Didn't selected																			

Table 2: Results obtained during the Dermic Sensitization evaluation in 50 volunteers.

Evaluation Days of the Areas in the Back after Patches Application Following the ICDRG Scale						
Nº Vol.	**Sensitization**					
	36th		38th		39th	
	A	B	A	B	A	B
01	-	-	-	-	-	-
02	-	-	-	-	-	-
03	-	-	-	-	-	-
04	-	-	-	-	-	-
05	-	-	-	-	-	-
06	-	-	-	-	-	-
07	-	-	-	-	-	-
08	-	-	-	-	-	-
09	-	-	-	-	-	-
10	-	-	-	-	-	-
11	-	-	-	-	-	-
12	-	-	-	-	Didn't return	
13	-	-	-	-	-	-
14	-	-	-	-	-	-
15	-	-	-	-	-	-
16	-	-	-	-	-	-
17	-	-	-	-	-	-
18	-	-	-	-	-	-
19	-	-	-	-	-	-
20	-	-	-	-	-	-
21	-	-	-	-	-	-
22	-	-	-	-	-	-
23	-	-	-	-	-	-
24	-	-	-	-	-	-
25	-	-	-	-	-	-
26	-	-	-	-	-	-
27	-	-	-	-	-	-
28	-	-	-	-	-	-
29	-	-	-	-	-	-
30	-	-	-	-	-	-
31	Didn't return					
32	-	-	-	-	-	-
33	-	-	-	-	-	-
34	-	-	-	-	-	-
35	-	-	-	-	-	-
36	-	-	-	-	-	-
37	Excluded					
38	-	-	-	-	-	-
39	-	-	-	-	-	-
40	-	-	-	-	-	-
41	-	-	-	-	-	-
42	-	-	-	-	-	-
43	-	-	-	-	-	-
44	-	-	-	-	-	-
45	-	-	-	-	-	-
46	-	-	-	-	-	-
47	-	-	-	-	-	-
48	-	-	-	-	-	-
49	-	-	-	-	-	-
50	-	-	-	-	-	-

Evaluation Days of the Areas in the Back after Patches Application Following the ICDRG Scale						
Nº Vol.	Sensitization					
	36th		38th		39th	
	A	B	A	B	A	B
51	-	-	-	-	-	-
52	-	-	-	-	-	-
53	-	-	-	-	-	-
54	Didn't selected					
55	Didn't selected					

Legend	
Areas	**Patches**
A	Negative Control
B	Product Tested

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: December 11, 2024

SUBJECT: Cocoyl Hydrolyzed Collagen

Anonymous. 2022. Repeated insult patch test (liquid blush containing 0.1% Cocoyl Hydrolyzed Collagen).

[redacted]

CLINICAL STUDY REPORT

Report Status	Final
Report Date	21 September 2022
[redacted]	[redacted]
[redacted]	[redacted]
Study Title	Repeated Insult Patch Test
Test Material	[redacted] liquid blush containing 0.1% Cocoyl Hydrolyzed Collagen
Sponsor	[redacted]
Sponsor Representative	[redacted]
Investigating Laboratory	[redacted]
Principal Investigator	[redacted], MD Diplomate, American Board of Dermatology
Study Initiation Date	25 May 2022
Study Completion Date	08 July 2022

PRINCIPAL INVESTIGATOR SIGNATURE

Study Title: Repeated Insult Patch Test

Clinical Study Number: [redacted]

I have read the study report and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

[redacted]

Principal Investigator Signature/Date

QUALITY ASSURANCE AUDIT STATEMENT

[redacted] follows established, standardized procedures for clinical testing designed to ensure the well-being of clinical study subjects and the generation of reliable study data. The study was conducted in accordance with the study protocol and [redacted] Standard Operating Procedures. In addition, the study was conducted following applicable ICH GCP standards to ensure reliability of data, subject safety and confidentiality. All data included in the report is accurately represented. The clinical study master file was reviewed by the Principal Investigator and the Quality Assurance representative.

[redacted]

Signature of QA Auditor and Date

1.0 ETHICS

1.1. ETHICAL CONDUCT OF THE STUDY

[redacted] follows established, standardized procedures for clinical testing designed to ensure the well-being of clinical study subjects and the generation of reliable study data. It is the responsibility of the Study Sponsor to ensure the study complies with applicable Drug, Cosmetic or Medical Device regulations, which vary by product. The Study Sponsor is solely responsible for product marketing claims based on its interpretation of [redacted] studies.

1.2. PARTICIPANT INFORMATION AND INFORMED CONSENT

Each subject was given a copy of the Informed Consent Form (ICF) had the nature and the purpose of the study explained to them by [redacted] personnel. Prior to entry into the study, the subject gave voluntary written consent to participate by signing the ICF. The Principal Investigator retains the original signed Informed Consent Form in the subject's file and gave a copy of the Informed Consent Form to the subject.

1.3. SUBJECT CONFIDENTIALITY

The Principal Investigator ensures that the research subject's confidentiality was maintained. Subjects are identified by their study ID number only. Documents are kept in strict confidence by the Principal Investigator. Any use of personally identifiable data or private health information must be justified by the Principal Investigator.

2.0 OBJECTIVE

The objective of this study was to determine the potential of a test material to elicit dermal irritation and/or induce sensitization following repeated patch applications.

3.0 TEST MATERIALS AND RECORD RETENTION

The test material received from the Sponsor was identified by [redacted] study and panel numbers. The test material was identified as follows:

Test Material	Test Condition	Patch Type
[redacted]	Tested as Received / Room Temperature	Occlusive

Product Information Table

[redacted]	[redacted]
Date sample made	5/3/2022
Expiration date	5/3/2023
Storage condition	Room Temperature

The Sponsor assumed responsibility for the purity, stability, characterization, and adequate preservation of the test materials. The Sponsor provided assurance that the test materials submitted were determined to be safe for use in humans.

3.1. STORAGE AND RETENTION

Test materials and study documentation will be retained as listed in the sponsor specific sample submission form.

4.0 SUBJECT SELECTION

A total of 120 male and female subjects, ranging in age from 18 to 70 years who met all of the inclusion criteria and none of the exclusion criteria as outlined in the study protocol, were selected for study participation.

5.0 STUDY EVALUATIONS

The following Dermal Scoring System was used:

Dermal Score	Description
0	No visible skin reaction
±	Barely perceptible erythema
1+	Mild erythema
2+	Well defined erythema
3+	Severe erythema and edema
4+	Erythema and edema with vesiculation

Letter Codes			
e = Edema	S = Spreading of reaction beyond patch site	D = Oozing, crusting, and/or superficial erosions	F = Follicular irritation with or without pustule formation (folliculitis)
P = Peeling	V = Vesiculation	d = Dryness/scaling	SD= Site Discontinued
Pa = Papules	B = Burning	Ho = Hypopigmentation	ST = Site Terminated
I = Itching	Sc = Scabbing	Hr = Hyperpigmentation	NP = No patching
X = Subject Absent	Ex = Excoriation	C = Changed Site	-- = No reading

6.0 TEST METHOD

This study was conducted according to clinical study protocol [redacted].

7.0 STUDY RESULTS

7.1. COMPLETED AND DISCONTINUED SUBJECTS

A total of 102 subjects completed the study. Discontinued subjects are listed below:

Subject Number	Reason for Discontinuation
19	Lost to Follow Up
28	Lost to Follow Up
29	Lost to Follow Up
34	Lost to Follow Up
35	Lost to Follow Up
47	Lost to Follow Up
57	Lost to Follow Up
62	Personal Reasons
64	Personal Reasons
69	Lost to Follow Up
72	Lost to Follow Up
76	Lost to Follow Up
79	Lost to Follow Up
96	Lost to Follow Up
98	Lost to Follow Up
106	Lost to Follow Up
107	Lost to Follow Up
110	Lost to Follow Up

7.2. DERMAL EVALUATIONS

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I for subjects that elicited dermal reactions, missed a visit, and/or were discontinued.

All other subjects did not exhibit any dermal reactions throughout the course of the entire study and had scores of '0'.

7.3. PROTOCOL DEVIATIONS

No protocol deviations occurred over the duration of the study.

7.4. PROTOCOL AMENDMENTS

There were no protocol amendments during this study.

7.0 STUDY RESULTS (CONTINUED)

7.5. ADVERSE EVENTS

No adverse events were reported over the duration of the study.

8.0 CONCLUSION

Based on the test population of 102 subjects and under the conditions of this study, the test material identified as [redacted] did not demonstrate a potential for eliciting dermal irritation or inducing sensitization.

Table I - Summary of Dermal Scores

Subject Number	Induction Scores									Challenge Scores			
	1	2	3	4	5	6	7	8	9	24 Hr.	48 Hr.	72 Hr.	96 Hr.
19	0	0	0	0	0	0	0	0	0	DISCONTINUED			
28	0	0	0	0	0	0	0	0	0	0	0	DISCONTINUED	
29	0	DISCONTINUED											
34	0	0	0	0	0	0	0	0	0	DISCONTINUED			
35	0	0	0	0	0	0	0	0	0	DISCONTINUED			
47	0	0	0	0	0	0	0	0	0	DISCONTINUED			
57	0	0	0	0	0	0	0	0	0	DISCONTINUED			
62	0	0	0	0	0	DISCONTINUED							
64	0	DISCONTINUED											
69	0	0	0	0	0	0	0	DISCONTINUED					
72	0	DISCONTINUED											
76	0	0	0	0	0	0	0	0	0	0	0	DISCONTINUED	
79	DISCONTINUED												
82	0	0	0	0	0	0	0	0	0	0	X	0	---
96	0	0	0	0	0	0	0	0	0	DISCONTINUED			
98	0	0	0	0	0	0	0	0	0	0	0	DISCONTINUED	
106	0	0	0	DISCONTINUED									
107	0	0	0	DISCONTINUED									
110	0	0	0	0	0	0	0	0	0	DISCONTINUED			

All other 101 subjects except the above listed did not exhibit any dermal reactions throughout the course of the entire study and had scores of '0'.

**All subjects started their challenge phase of the study on Tuesday 7/5/22 due to the holiday on Monday 7/4/22 (Independence Day). Due to this no subject received a 96-hour reading.

Appendix I - Subject Demographics

Subject Number	[redacted]
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Subject Number	[redacted]
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[redacted]

Appendix I – Subject Demographics (Continued)

Subject Number	[redacted]
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Subject Number	[redacted]
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Personal Care Products Council
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Memorandum

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

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

DATE: December 13, 2024

SUBJECT: Cocoyl Hydrolyzed Collagen Ingredients

Active Concepts. 2018. Dermal and ocular irritation tests AC Collagen Hydrolysate OS (Cocoyl Hydrolyzed Collagen).

Active Concepts recommends the following use concentrations:

Cocoyl Hydrolyzed Collagen	1-5%
Potassium Cocoyl Hydrolyzed Collage	1-10%

Dermal and Ocular Irritation Tests

info@activeconceptsllc.com • Phone: +1-704-276-7100 • Fax: +1-704-276-7101

Sample: AC Collagen Hydrolysate OS Cocoyl Hydrolyzed Collagen

Code: 20590

CAS #: 162353-78-8 or 68952-15-8

Test Request Form/Submission #: 4337

Lot #: 56523P

Sponsor: *Active Concepts, LLC; 107 Technology Drive Lincolnton, NC 28092*
Study Director: *Maureen Danaher*
Principle Investigator: *Jennifer Goodman*

Test Performed:
In Vitro EpiDerm™ Dermal Irritation Test (EPI-200-SIT)
EpiOcular™ Eye Irritation Test (OCL-200-EIT)

SUMMARY

In vitro dermal and ocular irritation studies were conducted to evaluate whether **AC Collagen Hydrolysate OS** would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays.

The product was tested according to the manufacture's protocol. The test article solution was found to be **non-irritating**. Reconstructed human epidermis and cornea epithelial model were incubated in growth media overnight to allow for tissue equilibration after shipping from MatTek Corporation, Ashland, MA. Test substances were applied to the tissue inserts and incubated for 60 minutes for liquid and solid substances in the EpiDerm™ assay and 30 minutes for liquid substances and 90 minutes for solid substances in the EpiOcular™ assay at 37°C, 5% CO_2, and 95% relative humidity (RH). Tissue inserts were thoroughly washed and transferred to fresh plates with growth media. After post substance dosing incubation is complete, the cell viability test begins. Cell viability is measured by dehydrogenase conversion of MTT [(*3-4,5-dimethyl thiazole 2-yl*)], present in the cell mitochondria, into blue formazan salt that is measured after extraction from the tissue. The irritation potential of the test chemical is dictated by the reduction in tissue viability of exposed tissues compared to the negative control.

Under the conditions of this assay, the test article was considered to be **non-irritant**. The negative and positive controls performed as anticipated.

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Dermal and Ocular Irritation Tests

I. Introduction

A. Purpose

In vitro dermal and ocular irritation studies were conducted to evaluate whether a test article would induce dermal or ocular irritation in the EpiDerm™ and EpiOcular™ model assays. MatTek Corporation's reconstructed human epidermal and human ocular models are becoming a standard in determining the irritancy potential of test substances. They are able to discriminate between irritants and non-irritants. The EpiDerm™ assay has accuracy for the prediction of UN GHS R38 skin irritating and no-label (non-skin irritating) test substances. The EpiOcular™ assay can differentiate chemicals that have been classified as R36 or R41 from the EU classifications based on Dangerous Substances Directive (DSD) or between the UN GHS Cat 1 and Cat 2 classifications.

II. Materials

A. Incubation Conditions:	37°C at 5% CO_2 and 95% relative humidity
B. Equipment:	Forma humidified incubator, ESCO biosafety laminar flow hood, Synergy HT Microplate reader; Pipettes
C. Media/Buffers:	DMEM based medium; DPBS; sterile deionized H_2O
D. Preparation:	Pre-incubate (37°C) tissue inserts in assay medium; Place assay medium and MTT diluent at 4°C, MTT concentrate at -20°C, and record lot numbers of kit components
E. Tissue Culture Plates:	Falcon flat bottom 96-well, 24-well, 12-well, and 6-well tissue culture plates
F. Reagents:	MTT (1.0mg/mL); Extraction Solution (Isopropanol); SDS (5%); Methyl Acetate
G. Other:	Nylon Mesh Circles (EPI-MESH); Cotton tip swabs; 1mL tuberculin syringes; Ted Pella micro-spatula; 220mL specimen containers; sterile disposable pipette tips; Parafilm

III. Test Assay

A. Test System

The reconstructed human epidermal model, EpiDerm™, and cornea epithelial model, EpiOcular™, consist of normal human-derived epidermal keratinocytes which have been cultured to form a multilayer, highly differentiated model of the human epidermis and cornea epithelium. These models consist of organized basal, spinous, and granular layers, and the EpiDerm™ systems also contains a multilayer stratum corneum containing intercellular lamellar lipid layers that the EpiOcular™ system is lacking. Both the EpiDerm™ and EpiOcular™ tissues are cultured on specially prepared cell culture inserts.

B. Negative Control

Sterile DPBS and sterile deionized water are used as negative controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

C. Positive Control

Known dermal and eye irritants, 5% SDS solution and Methyl Acetate, were used as positive controls for the EpiDerm™ and EpiOcular™ assays, respectfully.

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Dermal and Ocular Irritation Tests

D. Data Interpretation Procedure

a. EpiDerm™

An irritant is predicted if the mean relative tissue viability of the 3 tissues exposed to the test substance is reduced by 50% of the mean viability of the negative controls and a non-irritant's viability is > 50%.

b. EpiOcular™

An irritant is predicted if the mean relative tissue viability of the 2 tissues exposed to the test substance is reduced by 60% of the mean viability of the negative controls and a non-irritant's viability is > 40%.

IV. Method

A. Tissue Conditioning

Upon MatTek kit arrival at Active Concepts, LLC the tissue inserts are removed from their shipping medium and transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for 60 minutes. After those 60 minutes the inserts are transferred into fresh media and tissue culture plates and incubated at 37°C at 5% CO_2 and 95% relative humidity for an additional 18 to 21 hours.

B. Test Substance Exposure

a. EpiDerm™

30µL (liquid) or 25mg (solid) of the undiluted test substance is applied to 3 tissue inserts and allowed to incubate for 60 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

b. EpiOcular™

Each tissue is dosed with 20µL DPBS prior to test substance dosing. 50µL (liquid) or 50mg (solid) of the undiluted test substance is applied to 2 tissue inserts and allowed to incubate for 90 minutes in a humidified incubator (37°C, 5% CO_2, 95% RH).

C. Tissue Washing and Post Incubation

a. EpiDerm™

All tissue inserts are washed with DPBS, dried with cotton tipped swab, and transferred to fresh media and culture plates. After 24 hours the inserts are again transferred into fresh media and culture plates for an additional 18 to 20 hours.

b. EpiOcular™

Tissue inserts are washed with DPBS and immediately transferred into 5mL of assay medium for 12 to 14 minutes. After this soak the inserts are transferred into fresh media and tissue culture plates for 120 minutes for liquid substances and 18 hours for solid substances.

D. MTT Assay

Tissue inserts are transferred into 300µL MTT media in pre-filled plates and incubated for 3 hours at 37°C, 5% CO_2, and 95% RH. Inserts are then removed from the MTT medium and placed in 2mL of the extraction solution. The plate is sealed and incubated at room temperature in the dark for 24 hours. After extraction is complete the tissue inserts are pierced with forceps and 2 x 200µL aliquots of the blue formazan solution is transferred into a 96 well plate for Optical Density reading. The spectrophotometer reads the 96-well plate using a wavelength of 570 nm.

V. Acceptance Criterion

A. Negative Control

The results of this assay are acceptable if the mean negative control Optical Density (OD_{570}) is ≥ 1.0 and ≤ 2.5 (EpiDerm™) or ≥ 1.0 and ≤ 2.3 (EpiOcular™).

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Dermal and Ocular Irritation Tests

B. Positive Control

a. EpiDerm™

The assay meets the acceptance criterion if the mean viability of positive control tissues expressed as a % of the negative control is ≤ 20%.

b. EpiOcular™

The assay meets the acceptance criterion if the mean viability of positive control tissues is < 60% of control viability.

C. Standard Deviation

Since each irritancy potential is predicted from the mean viability of 3 tissues for EpiDerm™ and 2 tissues for EpiOcular™, the variability of the replicates should be < 18% for EpiDerm™ and < 20% EpiOcular™.

VI. Results

A. Tissue Characteristics

The tissue inserts included in the MatTek EpiDerm™ and EpiOcular™ assay kits were in good condition, intact, and viable.

B. Tissue Viability Assay

The results are summarized in Figure 1. In no case was the tissue viability ≤ 50% for EpiDerm™ or ≤ 60% for EpiOcular™ in the presence of the test substance. The negative control mean exhibited acceptable relative tissue viability while the positive control exhibited substantial loss of tissue viability and cell death.

C. Test Validity

The data obtained from this study met criteria for a valid assay.

VII. Conclusion

Under the conditions of this assay, the test article substance was considered to be **non-irritating**. The negative and positive controls performed as anticipated.

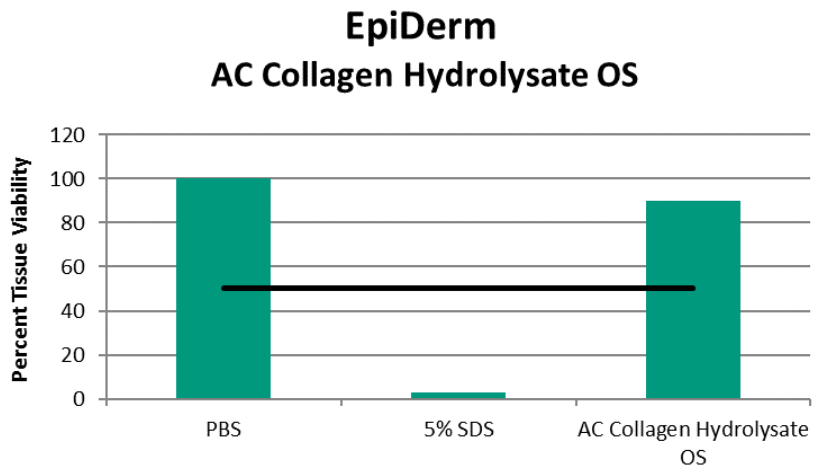

Figure 1: EpiDerm tissue viability

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Dermal and Ocular Irritation Tests

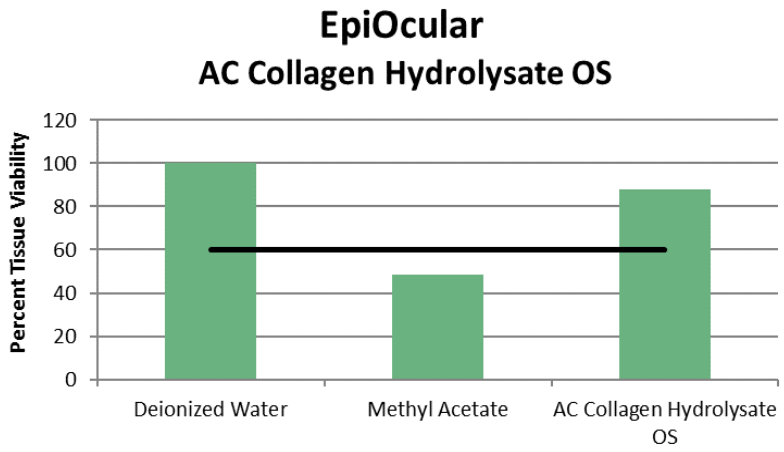

Figure 2: EpiOcular tissue viability

Personal Care Products Council
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Memorandum

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

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

DATE: January 27, 2025

SUBJECT: Potassium Cocoyl Hydrolyzed Collagen

Anonymous. 2001. Clinical safety evaluation repeated insult patch test (emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen tested as received).

[redacted]

[redacted]

FINAL REPORT

Clinical Safety Evaluation

Repeated Insult Patch Test

Test Article: [redacted]

Emulsion containing 0.058% Potassium Cocoyl Hydrolyzed Collagen tested as received

Submitted to:

[redacted]

Sponsor Code: [redacted]

[redacted]

Principal Investigator

4/11/01

Date of Final Report

[redacted]

Medical Investigator

QUALITY ASSURANCE STATEMENT

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in CFR 21, Part 50 (Protection of Human Subjects - Informed Consent) and Part 56 (Institutional Review Boards).

For Purposes of this clinical study:

_X__	Informed Consent was obtained.
_____	Informed Consent was not obtained.
_X__	An IRB review was not required.
_____	An IRB review was conducted and approval to conduct the proposed clinical research was granted.

This study report has been reviewed to assure that it correctly describes the methods of testing and that the reported results accurately reflect the data obtained during the clinical study ([redacted].

[redacted]
Quality Assurance Coordinator

4/10/01
Date

[redacted]

Clinical Safety Evaluation
Repeated Insult Patch Test

Objective:

To determine the irritation and/or sensitization potential of the test article after repeated applications under occlusive patch test conditions to the skin of human subjects (exclusive panel).

Investigator(s):

Principal Investigator: [redacted]
Medical Investigator: [redacted]

Testing Facility:

The study was conducted by [redacted]

Experimental Design:

Subject Selection

Sixty (60) subjects, 48 females and 12 males, ranging in age from 24 to 70 years were empanelled for this test.

The subjects were informed of the nature of the test, including possible adverse reactions. Written informed consent was obtained. Additionally, the subjects were considered dependable and able to read and understand instructions. The subjects did not exhibit any physical or dermatological condition that would have precluded application of the test article.

Test Article

The test article used in this study was provided by: [redacted]

It was received on February 13, 2001 and identified as follows:

[redacted] Code No.	Test Article I.D.	Description
[redacted]	[redacted]	White semi-viscous liquid

Method:

The Repeated Insult (occlusive) Patch Test (RIPT) was conducted as follows:

Induction Phase

The Induction Phase was initiated on February 21, 2001.

Approximately 0.2 ml of the test article was placed onto a 2-cm square occlusive patch (Parke-Davis Readi-Bandages), which was applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line.

The subjects were instructed to remove the patch 24-hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. The site was scored by a trained examiner just prior to the next patch application. In general, this procedure was repeated every Monday, Wednesday and Friday until nine (9) applications of the test article had been made.

Procedurally, if a subject developed a positive reaction of 2-level erythema or greater during the Induction phase or, at the discretion of the Principal Investigator, if the skin response warranted a change in site, the patch was applied to a previously unpatched, adjacent site for the next application. If a 2-level reaction (or greater) occurred at the new site, no further applications were made. However, all reactive subjects were subsequently Challenge patch tested.

Challenge Phase

After a rest period of approximately two weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. The site was scored 24 and 72-hours after application. All subjects were instructed to report any delayed skin reactivity that might have occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

The final Challenge patch reading was made on March 30, 2001.

Skin responses for both the Induction and Challenge phases of the study were scored according to the following 6-point scale:

0 = No evidence of any effect
+ = Barely Perceptible (Minimal, faint, uniform or spotty erythema)
1 = Mild (Pink, uniform erythema covering most of the contact site)
2 = Moderate (Pink-red erythema uniform in the entire contact site)
3 = Marked (Bright-red erythema with/without petechiae or papules)
4 = Severe (Deep-red erythema with/without vesiculation or weeping)

All other observed dermal sequelae (i.e., edema, dryness, papular responses, hypo- or hyper-pigmentation, etc.) were appropriately recorded and described as mild, moderate, or severe.

Results and Discussion:

(See Tables for Individual Scores)

Fifty-one (51) subjects satisfactorily completed the test procedure. Nine (9) test panelists discontinued for reasons unrelated to the conduct of the study. Discontinued panelists data are shown, up to the point of discontinuation, but are not used in the Results and Discussion or Conclusions sections of this final report.

Transient, barely-perceptible (+) non-specific patch test responses were observed on two (2/51) test panelists (Subject Nos. 36 and 52) during the Induction phase of the study. These responses were considered neither irritant nor allergic in nature.

No skin reactivity was observed during the Challenge Phase of the study.

Conclusions:

Under the conditions of a repeated insult (occlusive) patch test procedure with **Test Article:** [redacted] did not induce irritation, nor show any evidence of induced allergic contact dermatitis in human subjects.

[redacted]

Table I

[redacted]

RIPT (Occlusive)

[redacted]

Subject's Individual Scores

Subj. No.	Subj. Init.	Age	Sex	Induction Exposure No. 1	2	3	4	5	6	7	8	9	Challenge Reading (Hrs) 24	72
1	[redacted]	39	F	0	0	0	0	0	0	0	0	0	0	0
2		60	F	0	0	0	0	0	0	0	0	0	0	0
3		36	F	0	0	0	0	0	0	0	0	0	0	0
4		70	M	0	0	0	0	0	0	0	0	0	0	0
5		52	F	0	0	0	0	0	0	0	0	0	0	0
6		54	M	0	0	0	0	0	0	0	0	0	0	0
7		56	F	0	0	0	0	0	0	0	0	0	0	0
8		70	F	0	0	0	0	0	0	0	0	0	0	0
9		53	F	0	0	0	0	0	0	0	0	0	0	0
10		37	F	0	0	0	0	0	0	0	0	0	0	0
11		56	F	0	0	0	0	0	0	0	0	0	0	0
12		40	F	0	0	0	0	0	0	0	0	0	0	0
13		59	F	0	0	0	0	0	0	0	0	0	0	0
14		67	F	0	0	0	0	0	0	0	0	0	0	0
15		63	F	0	0	0	0	0	0	0	0	0	0	0
16		43	F	Disc										
17		35	F	0	0	0	0	0	0	0	0	0	0	0
18		44	F	0	0	0	0	0	0	0	0	0	0	0
19		24	M	0	0	0	0	0	0	0	0	0	0	0
20		31	F	0	0	0	0	0	0	0	0	0	0	0
21		42	F	0	0	0	0	0	0	0	0	0	0	0
22		28	F	0	Disc									
23		62	F	0	0	0	0	0	0	0	0	0	0	0
24		67	M	0	0	0	0	0	0	0	0	0	0	0
25		41	F	0	0	0	0	0	0	0	0	0	0	0
26		46	F	0	0	0	0	0	0	0	0	0	0	0
27		64	F	0	0	0	0	0	0	0	0	0	0	0
28		25	F	0	0	0	0	0	Disc					
29		48	F	0	0	0	0	0	0	0	0	0	0	0
30		31	F	0	0	0	0	0	0	0	0	0	0	0

Scale: 0 = No Reaction

Disc = Discontinued

\+ = Barely Perceptible (minimal, faint, uniform or spotty erythema)

1 = Mild (pink, uniform erythema covering most of the contact site)

2 = Moderate (pink-red erythema visibly uniform in entire contact site)

3 = Marked (bright-red erythema with/without petechiae or papules)

4 = Severe (deep-red erythema with/without vesiculation or weeping)

[redacted]

Table I

[redacted]

[redacted]

RIPT (Occlusive)

Subject's Individual Scores

Subj. No.	Subj. Init.	Age	Sex	Induction Exposure No. 1	2	3	4	5	6	7	8	9	Challenge Reading (Hrs) 24	72
31	[redacted]	43	F	0	0	0	0	0	0	0	0	0	0	0
32		30	F	0	0	0	0	0	0	0	0	0	0	0
33		66	M	0	0	0	0	0	0	0	0	0	0	0
34		67	F	0	0	0	0	0	0	0	0	0	0	0
35		70	M	0	0	0	0	0	0	0	0	0	0	0
36		39	M	+	0	0	+	0	+	+	+	+	0	0
37		25	F	0	0	0	Disc							
38		44	F	0	0	0	0	0	0	0	0	0	0	0
39		54	M	0	0	0	0	0	0	0	0	0	0	0
40		45	F	0	0	0	0	0	0	0	0	0	0	0
41		68	F	0	0	0	0	0	0	0	0	0	0	0
42		28	F	0	Disc									
43		50	F	Disc										
44		43	F	0	0	0	0	0	0	0	0	0	0	0
45		53	M	0	0	0	0	0	0	0	0	0	0	NR^
46		39	F	0	0	0	0	0	0	0	0	0	0	0
47		31	M	Disc										
48		30	F	0	0	0	0	0	0	0	0	0	0	0
49		52	F	0	0	0	Disc							
50		66	M	0	0	0	0	0	0	0	0	0	0	0
51		62	F	0	0	0	0	0	0	0	0	0	0	0
52		41	F	0	0	0	+	0	0	0	0	0	0	0
53		56	F	0	0	0	0	0	0	0	0	0	0	0
54		40	F	0	0	0	0	0	0	0	0	0	0	0
55		53	F	0	0	0	0	0	0	0	0	0	0	0
56		51	F	0	0	0	0	0	0	0	0	0	0	0
57		46	F	0	0	0	0	0	0	0	0	0	0	0
58		42	M	0	0	0	0	0	0	0	0	0	0	0
59		55	F	0	0	0	NR	0	0	0	0	0	0	0
60		42	F	0	0	0	0	Disc						

Scale:
0 = No Reaction
+ = Barely Perceptible (minimal, faint, uniform or spotty erythema)
1 = Mild (pink, uniform erythema covering most of the contact site)
2 = Moderate (pink-red erythema visibly uniform in entire contact site)
3 = Marked (bright-red erythema with/without petechiae or papules)
4 = Severe (deep-red erythema with/without vesiculation or weeping)

Disc = Discontinued
NR = No Read
^ 96 hr. read = 0

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: February 4, 2025

SUBJECT: Potassium Cocoyl Hydrolyzed Collagen

Anonymous. 2025. Summary information Potassium Cocoyl Hydrolyzed Collagen.

February 2025

Summary Information Potassium Cocoyl Hydrolyzed Collagen

A supplier reports that their Potassium Cocoyl Hydrolyzed Collagen product is prepared by condensation of coconut fatty acid and hydrolyzed collagen derived from fish scale.

	A number average molecular weight	Concentration	Impurities	
			Heavy metals	Arsenic
Potassium Cocoyl Hydrolyzed Collagen product	600	30% solution in water	Not more than 20 ppm	Not more than 2 ppm

Information Concerning Potassium Cocoyl Hydrolyzed Collagen product

Primary skin irritation
Mild irritant (rabbit, as is, 2002, OECD 404)

Test Animals:	New Zealand white rabbits (3 males)
Test Material:	Potassium Cocoyl Hydrolyzed Collagen product (as is)
Method:	Clipped intact skin and abraded skin of the back (2.5 x 2.5 cm) were treated with 0.5 mL of the test material, and the test site was occluded for 4 hours.
Observation:	Macroscopic evaluation (Draize classification method) at 24 and 72 hours after dosing.
Results:	A single 4-hour, semi-occluded application of the test material to the intact skin of three rabbits produced very slight to well-defined erythema and very slight oedema. One treated skin site appeared normal at the 72-hour observation and two remaining treated skin sites appeared normal at the 7-day observation.
Conclusion:	The test material produced a primary irritation index of 1.7 and was classified as MILD IRRITANT to rabbit skin according to the Draize classification scheme. No corrosive effects were noted.

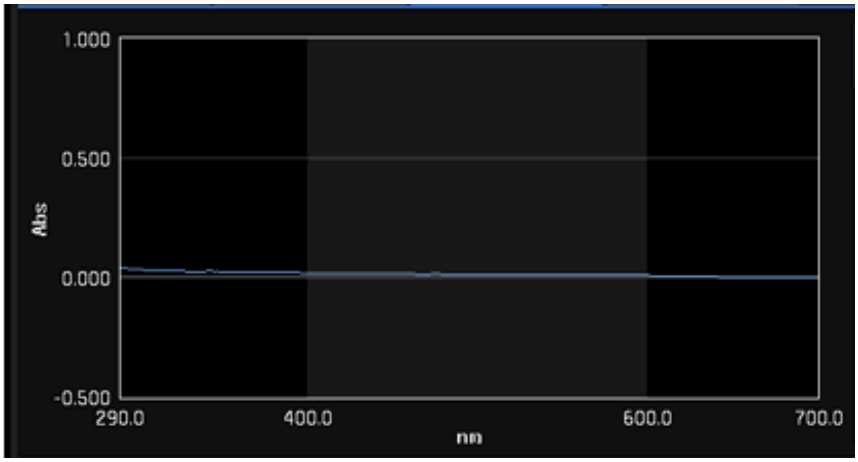
Dermal Irritation - Human
Non-irritant (Japanese, 25 subjects, as is, 2002)

The irritation potential of Potassium Cocoyl Hydrolyzed Collagen product was investigated in a 24 hours human patch test (occlusive) of 25 subjects (25 females). The backs of the subjects were treated with the test sample (Potassium Cocoyl Hydrolyzed Collagen product, as is) using Finn Chambers on Scanpor Tape. At 30-60 minutes and 24 hours after removal of the patch, any subjects did not have reaction.

Dermal Sensitization - Human (RIPT)
Non-sensitizer (50 subjects, as is, 2016)

Procedure:	0.2mL of the test material (Potassium Cocoyl Hydrolyzed Collagen product, as is) is dispensed onto the occlusive, hypoallergenic patch. The patch is applied directly to the skin of the infrascapular regions of the back. After 24 hours, the patch is removed. This procedure is repeated until a series of nine consecutive 24 hours exposures have been made for three consecutive weeks. Subjects are then given a 10-14 day rest period after which a challenge or retest dose is applied once to a previously unexposed test site. The retest dose is equivalent to any one of the original nine exposures. Reactions are scored 24 and 48 hours after application.
Results:	During the test, no clinically significant objective reaction was observed in any subjects.

UV absorption spectra
Test material: 0.1% dilution of Potassium Cocoyl Hydrolyzed Collagen product in purified water
Result: Test material does not have a Molar Extinction Coefficient (MEC) greater than 1000 L mol^{-1} cm^{-1} at any wavelength between 290 and 700 nm.



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Memorandum

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

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

DATE: February 11, 2025

SUBJECT: Potassium Cocoyl Hydrolyzed Collagen

Anonymous. 2025. CIR Support Potassium Cocoyl Hydrolyzed Collagen.

February 10, 2025

CIR Support Potassium Cocoyl Hydrolyzed Collagen

Sold to cosmetic manufacturers with following specifications:
Technical information

INCI name(s)
Potassium Cocoyl Hydrolyzed Collagen

Chemical description
Protein fatty acid condensate

Physical form:
Light-yellow to yellow, slightly viscous liquid with mild inherent odor

Characteristic values

The specifications stated in the paragraphs 'Quality control data' and 'Additional product descriptive data' finally and conclusively describe the properties of the product.

Quality control data
(Data which is used for quality release and is certified for each batch.)

Test property	Specification	Test method
Appearance at room temperature	Corresponds to the standard	AX-001001
Odor at room temperature	Corresponds to the standard	AX-001002
Dry substance	30.0 % - 33.0 %	CP-000016

Composition statement
INCI Components

INCI Name	Content
Potassium Cocoyl Hydrolyzed Collagen	20-40%
Aqua / Water	60-80%

INCI Name:
Potassium Cocoyl Hydrolyzed Collagen
Dry substance:
approx. 32%
Rec. Dosage:
5-20% as is

- Ultra mild anionic surfactant
- Improves skin and mucous membrane compatibility of surfactant preparations
- Good cleansing properties
- Particularly suitable for shampoos, body wash, bath preparations

Information on Toxicological Data

INCI name: Potassium Cocoyl Hydrolyzed Collagen

CAS : 68920-65-0

All studies described below were completed in 1977.

1) PRIMARY SKIN IRRITATION:

a) Undiluted **Not irritating** [1]

Method:
In reference to "Appraisal of the safety of chemicals in foods, drugs, and cosmetics," by the staff of the Division of Pharmacology, FDA, skin toxicity testing according to Draize (1959) was used. Primary skin irritation was measured using the patch test method on shaved and scarified skin of albino rabbits. According to this method, 0.5 ml of the undiluted test substance is secured to the skin using a patch measuring 2.5 x 2.5 cm. The animals are restrained in a holder, and the patch is affixed with the help of adhesive tape. The entire body of the animal is wrapped with a rubberized cloth for the exposure period of 24 hours to delay any potential evaporation of the test substances. After 24 hours, the patches are removed, and the local reaction is evaluated by scoring. Readings are repeated 72 hours after application, and the final score is determined as the average of the 24- and 72-hour readings. To ensure reproducibility of the values, two treated contact sites (shaved and shaved/scarified) and, as controls, two untreated contact sites (shaved and shaved/scarified) are established. Only reactions that are distinguishable from the control sites are considered positive skin reactions. The combined mean obtained is referred to as the primary irritation index. Compounds with a primary irritation index of 2 or less are classified as mild irritants, those with an index of 2 to 5 as moderate irritants, and those above 6 as severe irritants.

Animals:
Six adult albino rabbits (New Zealand Whites) with an average weight of 2.5 kg were used. The animals were kept in individual cages and were fed a standard rabbit diet (Hâing 222) along with water ad libitum. The room temperature during the test period ranged from 20 °C to 10 °C (maximum limit), and the relative humidity was 50% to 60%. The lighting duration was 12 hours per day.

Results:
Potassium Cocoyl Hydrolyzed Collagen was tested undiluted for primary skin irritation in rabbits. Under the described experimental conditions, a pronounced erythema was observed on the shaved and shaved/scarified skin of all animals after 24 hours. The reported skin changes were still present in a diminished form in 5 animals after 72 hours. The primary irritation index was 1.59. The preparation is classified as a "mild irritant" in the tested form (according to Draize, 1959).

b) Diluted **Not irritating** [2]

Method:
Potassium Cocoyl Hydrolyzed Collagen was tested in diluted form (10% active matter) according to the protocol described in the paragraph before.

Results:
Potassium Cocoyl Hydrolyzed Collagen was diluted to 10% in distilled water and subjected to a test for primary skin irritation in rabbits. Under the described experimental conditions, it was found that the preparation did not cause any changes on the skin of albino rabbits in terms of dermatitis, erythema, or edema formation. The primary irritation index was 0. The preparation is classified in the tested form as "no irritant."

2) SENSITIZATION: **Not sensitizing [3]**

Method:
Potassium Cocoyl Hydrolyzed Collagen (30% active matter) was tested according to the Buehler protocol. 10 treated and 5 control Pirbright guinea pigs were used. The treatment was administered once a week for 3 weeks. Fourteen days after the last treatment, all 15 animals were subjected to retesting on the right flank. After 6 hours, the patches were removed. Twenty-four hours later, all animals were depilated with a depilatory agent, and the skin reaction was assessed using the Draize scale 2, 24, and 48 hours after depilation.

Results:
Potassium Cocoyl Hydrolyzed Collagen (30% active matter) was tested as a 10% solution in distilled water in a closed epicutaneous test for contact hypersensitivity of the skin. Under the given experimental conditions, no contact hypersensitivity was demonstrated for the substance as a 10% solution in distilled water.

3) PHOTOSENSITIZATION: **Not photosensitizing [4]**

To test the photosensitizing properties of Potassium Cocoyl Hydrolyzed Collagen (9% active matter), 40 Pirbright guinea pigs (10 males and 10 females for the test group and the control group) were used. Any reactions occurring on the skin were assessed 2, 6, and 24 hours after retesting, as well as 2, 6, 24, and 48 hours after depilation. The animals showed normal weight development throughout the entire testing period.
No photosensitizing effect was observed for the substance Potassium Cocoyl Hydrolyzed Collagen in guinea pigs.

Concentration of Use by FDA Product Category[1]*

Cocoyl Hydrolyzed Collagen
Potassium Cocoyl Hydrolyzed Collagen
Sodium Cocoyl Hydrolyzed Collagen
TEA-Cocoyl Hydrolyzed Collagen

Ingredient	Product Category	Maximum Concentration of Use
Potassium Cocoyl Hydrolyzed Collagen	Face and neck products (not spray) – leave-on	0.01%
Sodium Cocoyl Hydrolyzed Collagen	Other personal cleanliness products – rinse-off	1.1%

*The ingredients included in the title of the table but not found in the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2025
Table prepared: March 27, 2025

[1] The new FDA cosmetic product categories under MoCRA were used for this survey.