Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	August 20, 2021
Panel Meeting Date:	September 13 – 14, 2021

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Priya Cherian, Scientific Analyst/Writer, CIR.

1620 L Street, NW, Suite 1200 ◇ Washington, DC 20036-4702 ◇ ph 202.331.0651 ◇ fax 202.331.0088 ◇
cirinfo@cir-safety.org

Cosmetic Ingredient Review

Commitment & Credibility since 1976

Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Priya Cherian, Scientific Analyst/Writer, CIR
Date: August 20, 2021
Subject: Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Tentative Report of the Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics (*sugarc092021rep*). The 4 ingredients included in this report are Saccharum Officinarum (Sugarcane) Bagasse Powder, Saccharum Officinarum (Sugarcane) Extract, Saccharum Officinarum (Sugarcane) Juice Extract, and Saccharum Officinarum (Sugarcane) Wax.

At the December 2020 meeting, the Expert Panel for Cosmetic Ingredient Safety (Panel) issued an Insufficient Data Announcement for this ingredient group, and requested irritation and sensitization data on Saccharum Officinarum (Sugarcane) Extract at the reported maximum use concentration of 2.4%. Since the December Panel meeting, unpublished data have been received and incorporated (highlighted in yellow in the report document). These data include:

- A 21-d cutaneous tolerance assay on a rinse-off face mask formulation containing 0.36% Saccharum Officinarum (Sugarcane) Extract, performed on 21 subjects (*sugarc092021data1*)
- A human repeat insult patch test (HRIPT) performed on 105 subjects using a facial serum containing 1.44% Saccharum Officinarum (Sugarcane) Extract (*sugarc092021data2*)
- An HRIPT performed on 105 subjects using a facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract (*sugarc092021data3*)

Also included in this package for your review are the report history (*sugarc092021hist*), flow chart (*sugarc092021flow*), literature search strategy (*sugarc092021strat*), updated data profile (*sugarc092021prof*), minutes (*sugarc092021min*) and 2021 VCRP data (*sugarc092021FDA*).

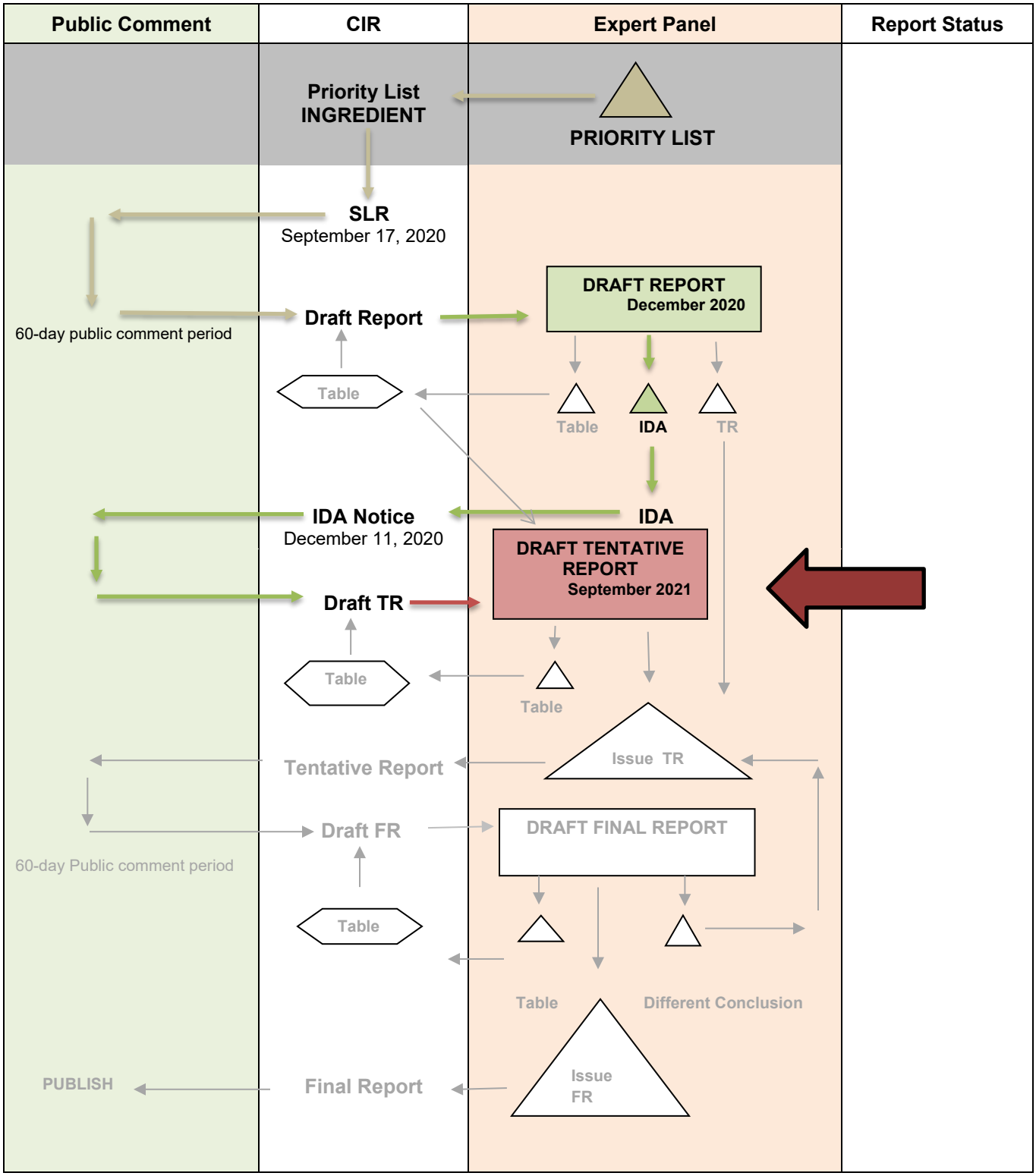
The Panel should carefully consider and discuss the data (or lack thereof), and the draft Abstract and draft Discussion presented in this report. A Tentative Report with a safe, safe with qualifications, unsafe, insufficient data, or split conclusion should then be issued.

1620 L Street, NW Suite 1200, Washington, DC 20036
(Main) 202-331-0651 (Fax) 202-331-0088
(email) cirinfo@cir-safety.org (website) www.cir-safety.org

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY *Saccharum officinarum* (Sugarcane)-derived ingredients

MEETING September 2021



Saccharum officinarum (sugarcane) – derived ingredients – History

March 2019

- 2 new additional ingredients added to report: Saccharum Officinarum (Sugarcane) Bagasse Powder and Saccharum Officinarum (Sugarcane) Juice Extract

July 2019

- Concentration of use data received for Saccharum Officinarum (Sugarcane) Extract and Saccharum Officinarum (Sugarcane) Wax

September 2020

- SLR posted
- Comments on SLR received from PCPC

October 2020

- Manufacturing and physiochemical properties data on Saccharum Officinarum (Sugarcane) Extract received
- Concentration of use information received for the 2 additional ingredients (Saccharum Officinarum (Sugarcane) Juice Extract and Saccharum Officinarum (Sugarcane) Bagasse Powder)

December 2020

- The Expert Panel on Cosmetic Ingredient Safety (Panel) reviews the Draft Report and issues an IDA; requests irritation and sensitization data on all ingredients at max use concentration of 2.4%
- Comments on Draft Report received from PCPC

January 2021

- Cutaneous tolerance data received from PCPC – 21-d cutaneous tolerance assay on rinse-off face mask formulation containing 0.36% Saccharum Officinarum (Sugarcane) Extract
- HRIPT data received from PCPC – facial serum containing 1.44% Saccharum Officinarum (Sugarcane) Extract

February 2021

- HRIPT data received from PCPC – facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract

September 2021

- The Expert Panel reviews the Draft Tentative Report

Saccharum officinarum (Sugarcane)-Derived Ingredients Data Profile – September 2021 – Priya Cherian, Scientific Analyst/Writer																													
						Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies	
	Reported Use	GRAS	Method of Mfg	Constituents	Impurities	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Saccharum Officinarum (Sugarcane) Extract	X		X	X																		X			X				
Saccharum Officinarum (Sugarcane) Bagasse Powder				X																									
Saccharum Officinarum (Sugarcane) Juice Extract	X		X	X	X				X																				
Saccharum Officinarum (Sugarcane) Wax	X		X	X																									
Saccharum Officinarum (Sugarcane) higher aliphatic primary acids*									X			X			X		X		X										
Saccharum Officinarum (Sugarcane) long chain primary alcohols*				X								X							X										

"X" indicates that data were available in a category for the ingredient

* data provided are on major components of sugarcane wax (higher aliphatic primary acids or long-chain primary alcohols), however, they are not a specified ingredient being reviewed in this report

Sugarcane-derived Ingredients Search Strategy

Ingredient	CAS #	InfoB	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Saccharum Officinarum (Sugarcane) Bagasse Powder		✓	✓			✓													✓
Saccharum Officinarum (Sugarcane) Extract	91722-22-4	✓	✓			✓													✓
Saccharum Oficinarum (Sugarcane) Juice Extract	91722-22-4	✓	✓			✓													✓
Saccharum Officinarum (Sugarcane) Wax	142583-61-7	✓	✓			✓													✓

Search Strategy

[*document search strategy used for SciFinder, PubMed, and Toxnet*]

Saccharum officinarum
Sugarcane toxicity
Sugarcane dermal
Sugarcane extract
Sugarcane wax
Sugarcane penetration
Sugarcane composition
Sugarcane cosmetic
Bagasse
Sugarcane pesticides
Sugarcane impurities
D-003 toxicity
Policosanol toxicity
CAS numbers
Sugarcane metabolism
Sugarcane carcinogenicity
Sugarcane tumor
Sugarcane cancer

LINKS

Search Engines

- Pubmed (- http://www.ncbi.nlm.nih.gov/pubmed)
- Toxnet (https://toxnet.nlm.nih.gov/); (includes Toxline; HSDB; ChemIDPlus; DART; IRIS; CCRIS; CPDB; GENE-TOX)

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

Pertinent Websites

- wINCI - http://webdictionary.personalcarecouncil.org
- FDA databases http://www.ecfr.gov/cgi-bin/ECFR?page=browse
- FDA search databases: http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm;,
- EAFUS: http://www.accessdata.fda.gov/scripts/fcn/fcnnavigation.cfm?rpt=eafuslisting&displayall=true
- GRAS listing: http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm
- SCOGS database: http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm
- Indirect Food Additives: http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives
- Drug Approvals and Database: http://www.fda.gov/Drugs/InformationOnDrugs/default.htm
- http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/UCM135688.pdf
- FDA Orange Book: https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm
- OTC ingredient list: https://www.fda.gov/downloads/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cder/ucm135688.pdf
- (inactive ingredients approved for drugs: http://www.accessdata.fda.gov/scripts/cder/iig/
- HPVIS (EPA High-Production Volume Info Systems) - https://ofmext.epa.gov/hpvis/HPVISlogon
- NIOSH (National Institute for Occupational Safety and Health) - http://www.cdc.gov/niosh/
- NTIS (National Technical Information Service) - http://www.ntis.gov/
- NTP (National Toxicology Program) - http://ntp.niehs.nih.gov/
- Office of Dietary Supplements https://ods.od.nih.gov/
- FEMA (Flavor & Extract Manufacturers Association) - http://www.femaflavor.org/search/apachesolr_search/
- EU CosIng database: http://ec.europa.eu/growth/tools-databases/cosing/
- ECHA (European Chemicals Agency – REACH dossiers) – http://echa.europa.eu/information-on-chemicals;jsessionid=A978100B4E4CC39C78C93A851EB3E3C7.live1
- ECETOC (European Centre for Ecotoxicology and Toxicology of Chemicals) - http://www.ecetoc.org
- European Medicines Agency (EMA) - http://www.ema.europa.eu/ema/
- IUCLID (International Uniform Chemical Information Database) - https://iuclid6.echa.europa.eu/search
- OECD SIDS (Organisation for Economic Co-operation and Development Screening Info Data Sets)- http://webnet.oecd.org/hpv/ui/Search.aspx
- SCCS (Scientific Committee for Consumer Safety) opinions: http://ec.europa.eu/health/scientific_committees/consumer_safety/opinions/index_en.htm
- NICNAS (Australian National Industrial Chemical Notification and Assessment Scheme)- https://www.nicnas.gov.au/
- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

Botanical Websites, if applicable

- Dr. Duke's - https://phytochem.nal.usda.gov/phytochem/search
- Taxonomy database - http://www.ncbi.nlm.nih.gov/taxonomy
- GRIN (U.S. National Plant Germplasm System) - https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx
- Sigma Aldrich plant profiler- http://www.sigmaaldrich.com/life-science/nutrition-research/learning-center/plant-profiler.html
- American Herbal Products Association Botanical Safety Handbook (database) - http://www.ahpa.org/Resources/BotanicalSafetyHandbook.aspx
- European Medicines Agency Herbal Medicines - http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/landing/herbal_search.jsp
- National Agricultural Library NAL Catalog (AGRICOLA) https://agricola.nal.usda.gov/
- The Seasoning and Spice Association List of Culinary Herbs and Spices
- http://www.seasoningandspice.org.uk/ssa/background_culinary-herbs-spices.aspx

Fragrance Websites, if applicable

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM)

DECEMBER 2020 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito Team – December 7, 2020

DR. BELSITO: So sugarcane. So this is the first time we're looking at this safety assessment. And let's see what we got here. So it has some quercetin it, but I don't think that was important. On PDF Page 10, where it says during the harvesting season, that last area that talks about the benzanthracene with fluoranthene, the benzopyrene, do we want to say anything about that?

DR. LIEBLER: I flagged that also. I think that's actually interesting and relevant. On their conditions of harvest, there's often burning of fields going on and this yields carcinogens that could contaminate the product. And so, I think it should be a discussion point. And that industry should take efforts to minimize the concentration of combusted products contaminants.

DR. BELSITO: Okay. That's what I had too. Just Curt, Paul, are you good with that?

DR. KLAASSEN: I'm fine.

DR. SNYDER: Yeah. I'm actually reading a book about the history of the sugarcane industry in Florida post the Cuban embargo. It's pretty interesting. And it's amazing to see them burn the fields down here. It's crazy.

DR. BELSITO: Yeah. It is. I actually saw that in Dominican Republic.

DR. LIEBLER: Is it a big, huge, smoke mess?

DR. SNYDER: It is a humongous mess.

DR. BELSITO: Yeah.

DR. LIEBLER: They used to burn the fields in Oregon after the grass harvest when I first got out there when I did my post doc. And they actually had huge multi-car pile ups on interstate when it'd get covered up in smoke. And they actually had to stop doing that. I don't think they stopped it in the sugarcane, though.

DR. SNYDER: The first time I asked somebody about why do they do it, they said to get rid of the snakes. But I've learned subsequently that's not the reason they do.

DR. LIEBLER: Oh, thank you. Priya, put in the snake boilerplate, please.

DR. BELSITO: Okay. So are we satisfied with the composition, manufacturing impurities, or do we need more hard data?

DR. SNYDER: No. I thought it was good.

DR. BELSITO: Okay. And I think the wax is okay given the chronic oral tox and the DART. But we don't have sensitization and irritation on the wax. Do we need that?

DR. SNYDER: That was my only flag, was irritation and sensitization.

DR. LIEBLER: Yeah. The wax is unlikely to contain most of this sort of skin reactive chemical constituents. And it does mention some aldehydes, I guess. But it's a very nonpolar group.

DR. BELSITO: Okay. So we're asking for sensitization and irritation at concentration of use?

DR. SNYDER: Two point four percent max.

DR. LIEBLER: Yeah.

DR. BELSITO: Yeah. For which ingredient?

DR. LIEBLER: What's the most used?

DR. SNYDER: The extract.

DR. LIEBLER: The extract? That's a whole plant, right?

DR. SNYDER: Yeah.

DR. BELSITO: Okay. So sensitization and irritation at use concentration for the whole extract?

DR. LIEBLER: Yeah. Yeah. I think that would cover the others.

DR. BELSITO: Okay. Do we need a 28-day dermal or since this is a food?

DR. LIEBLER: No. I think it's widely consumed.

DR. SNYDER: And we have tables of data, Tables 4 and 5, I believe.

DR. BELSITO: Okay. So basically, all we're asking for is sensitization and irritation at concentration of use for the whole extract. And the discussion will be the respiratory boilerplate, the botanical boilerplate, and the contaminants that come from burning the fields.

DR. SNYDER: Yes.

DR. LIEBLER: Right.

DR. BELSITO: Okay. Anything else? No?

DR. BELSITO: Priya, are you all set there?

MS. CHERIAN: I am all set, thank you.

DR. BELSITO: Okay. Well, I think we're done now.

DR. SNYDER: Yes.

DR. LIEBLER: Very nice.

DR. SNYDER: Tacos at 4:00.

DR. BELSITO: I just have a question, Monice. On the documents that Bart sent, there was one on rosa whatever. Why was that sent?

DR. LIEBLER: Yes.

MS. FIUME: Which -- I'm sorry, Don, which document?

DR. BELSITO: His last note saying he received some late stuff. It freaked me out and made me think that I had forgotten an ingredient.

DR. LIEBLER: I think there must be upcoming ingredients.

MS. FIUME: That will be at the next meeting. So they were probably comments that were inadvertently sent on that.

DR. LIEBLER: There were council comments -- council comments on Rosa D flower, water and oil.

DR. BELSITO: Yeah.

MS. FIUME: Yeah. That will be coming up in the next meeting. So they were probably just inadvertently sent. Sorry about that.

DR. BELSITO: No. That's okay. Great. Thank you. Well, we'll see you all tomorrow. For those of you who Bart sends a breakfast to, it'll be 8:00. Otherwise, it'll be 8:30.

DR. LIEBLER: Okay.

DR. BELSITO: Okay. Have a great afternoon.

MS. FIUME: See you all tomorrow. Have a nice night.

DR. BELSITO: Okay. Thanks, bye bye.

MS. FIUME: Bye bye.

DR. KLAASSEN: Bye bye.

Cohen Team – December 7, 2020

DR. COHEN: Go to sugarcane. Okay. Saccharum officinarum, sugarcane-derived ingredients. This is Priya's as well. This is a draft report. This is the first time we're reviewing this and the safety assessment has four derived ingredients, which is the Bagasse powder, extract, juice extract, and wax. We have some others on the table for read across.

It's a skin-conditioning agent. It's also used as a surfactant, exfoliant, solvent, deodorant, binder, protectant, and emulsion stabilizer. Max use of 0.5 percent in a rinse-off product and 2.4 percent in a leave-on foot powder. Frequency of use as reported. There's no apparent uses for the Bagasse, and there is some concentrations of use reported for the wax and juice.

In 2019, the Panel reviewed mono- and diglycerides including sucrose as safe in the present practice. Let's see. We have method of manufacturing on everything but the Bagasse Powder, so comments?

DR. PETERSON: I actually think we might have the method of manufacture for Bagasse because, when you look multiple places on the internet, it's basically what's left over after the juice is removed. So it's that debris. You know, they take the juice out, and it's what's left over. So, I guess, my question was, is that actually a method of manufacturing that could be stated?

DR. COHEN: Well, there may be some processing of it --

DR. PETERSON: Right.

DR. COHEN: -- that we don't know about, right --

DR. PETERSON: Okay. Right.

DR. COHEN: -- to make it a powder, right? I just don't know.

DR. PETERSON: Okay.

DR. COHEN: So other -- Lisa, any -- what else do you need?

DR. PETERSON: Well, there weren't impurities listed for the extract. The sugarcane extract, there were no impurities for that, the powder, or the wax. And then method of manufacturing for the Bagasse powder. So, yeah. Just the impurities and the one method of manufacturing were the insufficiencies that I identified. I mean, there's also no dermal sensitization --

DR. COHEN: Yeah.

DR. PETERSON: -- but I'll stick to my lane, which is the chemistry.

DR. COHEN: I don't know. Ron?

DR. SHANK: Okay. The sugarcane and the sugarcane extract are foods, so we don't need any more systemic tox data. We should request dermal sensitization on the sugarcane extract at its highest use concentration, which is 2.4 percent in a leave on.

The wax is used at a very low concentration in rinse-off products, so, I think, it's very unlikely that that would penetrate the stratum corneum. So I don't see any tox needs for sugarcane wax. And that's all.

DR. COHEN: What about the irritation/sensitization?

DR. SHANK: On the sugarcane extract?

DR. COHEN: No the wax.

DR. SHANK: Not the wax, no.

DR. SLAGA : On the extract, yeah.

DR. COHEN: Okay. There are --

DR. SHANK: But, if the dermatologists want the sensitization on the wax, okay. I don't know.

DR. COHEN: I think I do.

DR. SHANK: Okay.

DR. COHEN: There is some discussion about hypersensitivity reactions to sugarcane pollen. These were immediate-type hypersensitivity reactions, but I don't anticipate that crosses over into what we're looking at right now. But is that a concern or possibility?

DR. SHANK: The pollen?

DR. COHEN: Yeah.

DR. SHANK: No, not to me.

DR. COHEN: Okay. Priya, I found it very strange -- I could not get the translation, but I found two cases of dermatitis in workers in sugarcane fields in the *Journal of the Italian Society of Occupational Medicine* from the early 1950's. I've seen nothing since then, so I don't think that there's anything major going on. I can send you the PubMed link on that.

MS. CHERIAN: Okay. Please do.

DR. COHEN: So, Tom, anything else?

DR. SLAGA : No, actually, which we don't need, but there was carcinogenic data. It was negative. And actually it has some positive anti-carcinogenic activity too. I believe the wax is the one they tested.

DR. COHEN: Yeah.

DR. SLAGA : We don't need that, but I just want to -- it's not very often if we didn't --

DR. BERGFELD: We haven't seen that before. Tom, did you -- I don't think we've seen that before.

DR. COHEN: What was that, Wilma? What was that?

DR. BERGFELD: I don't think we've seen that before, the anti-carcinogenic activity. If we have, it's been a very --

DR. SLAGA : Well, it has -- it's non-carcinogenic as well as anti, so that gives you even a greater sense that it's safe.

DR. BERGFELD: Right. Right.

DR. SLAGA : And actually it -- anyway, I just wanted to -- it's nice to get some data once in a while that even though you don't need it in this case.

DR. COHEN: So we'll have insufficient data for the extract powder and wax for impurities. Method of manufacturing for the Bagasse powder, dermal, irritation and sensitization for the extract at highest use, and for the wax.

DR. SHANK: Okay.

DR. COHEN: Is that --

DR. SHANK: That's okay with me.

DR. COHEN: Any other?

DR. PETERSON: Nope.

DR. SLAGA : Okay with me.

DR. COHEN: Procedurally, is there anything else on this?

DR. HELDRETH: No, since it's a draft report, and especially since it's a botanical source, typically, you'll just put out an IDA. There's no need to make a conclusion at this point. Just a list of needs so that the Panel can move forward the next time they see it.

DR. BERGFELD: Could we make a little bit of a comment on the discussion, what it will contain?

DR. HELDRETH: That would be wonderful.

DR. BERGFELD: Well, one of -- Ron could talk to this, but it's table sugar, the food. And then the IGE sensitization, I think, needs to be added. And then the (audio skip) of human irritation/sensitization and even eye. And then the impurities for -- which one was that? Let me see. The extract.

DR. COHEN: Extract powder and wax.

DR. SHANK: Are you asking a question?

DR. BERGFELD: No, is there anything else that needs to go into the discussion? I was just listing some of the things I saw.

DR. SHANK: Not just the --

DR. COHEN: I think the sugarcane pollen allergy issue is important to put in there.

DR. BERGFELD: Yeah. Right. The IGE. I guess there are no others.

DR. COHEN: Okay. They'll probably evolve as we go along. Okay. The next one is tea tree.

Full Panel – December 8, 2020

DR. COHEN: Okay, so, Saccharum officinarum, sugarcane, there are four derived ingredients; it's the Bagasse Powder, Extract, Juice Extract, and Wax. This is the first time we're reviewing this, and it has a max of 0.5 percent in rinse-off products, and 2.4 percent in a leave-on foot powder. The group reviewed mono- and disaccharides as safe in present practices of use and concentration, including sucrose, in 2019.

Our group concluded, with incomplete data for method of manufacturing for Bagasse, impurities for Extract, Powder and Wax, and irritancy and sensitization for the Extract at the highest concentration of use, and the Wax.

DR. BERGFELD: Is there a second or comment?

DR. BELSITO: Well, we agreed with sensitization and irritation of concentration of use for the whole extract. We also had some concern about contaminants that could occur from burning the sugarcane and that would go in the discussion.

I think overall our group was satisfied with composition, manufacturing and impurities, and did not need additional hard data, but I'll let Dan address that.

DR. LIEBLER: I think the point was made it was the Bagasse, the sugarcane stalk. And it might be the most brief description of method of manufacturer we have. Actually, it's composition and impurities on PDF 10, it says "crushed sugarcane stalk." So, I got that. That's a method of manufacture.

DR. PETERSON: I pointed that out in my group and I was told it wasn't sufficient because it doesn't -- it has to then get created into a powder. But I agree with you.

DR. BERGFELD: Ron?

DR. LIEBLER: Well, obviously the other people on your team don't know the first thing about crushing sugarcane stalks.

DR. BERGFELD: Ron and Tom, you want to comment?

DR. SHANK: No.

DR. SLAGA: I have no problem with it either.

DR. BERGFELD: Okay. Ron?

DR. COHEN: Um --

DR. BERGFELD: Go ahead David.

DR. COHEN: Don, for the irritancy and sensitization for the Extract, I think, that makes sense. The reason to put in the Wax, was it makes up a very small percentage of the total plant. And, recent -- the report, it indicates that there're esters and aldehydes, and ketones. And I wasn't clear whether that could be a more concentrated product that could create a sensitization issue with the aldehydes.

DR. BELSITO: We discussed the Wax, and Dan I think you had comments on why that wasn't an issue. Do you want to address that again?

DR. LIEBLER: Yeah, I mean, you're right, David. The functional groups potentially are alerts, but these are going to very long chain aldehydes, ketones to the extend they are along with other very long chain materials that are probably not going to be absorbed. So that was the reason I had less concern about the Wax.

DR. BERGFELD: Okay. Lisa, you want to respond?

DR. PETERSON: No, I don't have any response.

DR. BERGFELD: You're agreeing?

DR. PETERSON: Yeah, I think so. I mean, again, there's a lot of -- a little hand waving, but I think that -- yeah, I always err on the side of data. But I --

DR. BERGFELD: Okay. Anyone else?

DR. PETERSON: If we're asking for insufficiencies, why not add that and just see what we get?

DR. LIEBLER: Well, I don't object to that for certain.

DR. SHANK: The Wax is used at the very low concentration in rinse-offs.

DR. PETERSON: Okay, then it's not going to be a concern. Yeah, you're right.

DR. COHEN: Okay, so, as far as the comments for method of manufacturing, we're okay keeping. But impurities, you feel we have enough?

DR. BELSITO: We're not even asking for manufacturing.

DR. COHEN: But -- well, again, we -- you're group's assertion of me not being familiar with the crushing of sugarcane, stems from my growing up in southern Brooklyn where we didn't really do a lot of sugarcane crushing.

DR. BELSITO: I think maybe the Panel needs to take a trip to DR and see how they actually make the Bagasse.

DR. COHEN: I'll be there. Anyone from our group, Ron, Tom, Lisa, about removing method of manufacturing for Bagasse? Ron?

DR. SHANK: I don't feel strongly about it at all. I don't think it's important, but if you want to put it in, fine.

DR. SLAGA: I don't think we need it either.

DR. BELSITO: And, impurities, for the Extract, Powder and Wax?

DR. SHANK: You can probably use your boilerplate for metals and pesticides.

DR. SLAGA: Right.

DR. COHEN: Okay, yeah, that makes sense.

DR. BERGFELD: In the discussion.

DR. COHEN: Okay. So, I'd like to rescind my last motion and create a new motion for an incomplete data, requesting irritancy and sensitization data for the highest concentration of use for the extract.

DR. BERGFELD: That's the second, Dan? Don?

DR. BELSITO: Second.

DR. BERGFELD: Any other discussion? This is going IDA. This is an insufficient data announcement.

DR. BELSITO: So as we create the discussion, we need the respiratory boilerplate, the botanical boilerplate, the discussion about potential PAH contaminants that could occur as a result of burning the field.

DR. BERGFELD: Oh, interesting. And you came up -- just out of curiosity, you came up with burning the field from where?

DR. BELSITO: From the fact that that's what they often do. They burn the fields --

DR. BERGFELD: But do they harvest first, though, Don't they?

DR. BELSITO: Well, there can be considerable contamination of the product from the smoke that's generated as a result of that. So we just thought to err on the side of safety, that good manufacturing processes would assure that the amount of PAH would be limited.

DR. LIEBLER: It was discussed on PDF Page 10.

DR. BERGFELD: Okay. So we have a second and we have our list, and we've just added a couple of items, PAH as being one. Any other items that need to be discussed or boilerplated into the discussion?

Seeing none, I'm going to call for the question. All those oppose of moving forward with an IDA on this ingredient, please indicate by stating your name. Then, I assume everyone is unanimous -- this is approved unanimously. So, moving on to the next item, Dr. Belsito on Papaya.

Safety Assessment of *Saccharum officinarum* (Sugarcane)-Derived Ingredients as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	August 20, 2021
Panel Meeting Date:	September 13 – 14, 2021

The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The Cosmetic Ingredient Review (CIR) Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Priya Cherian, Scientific Analyst/Writer, CIR.

1620 L Street, NW, Suite 1200 ♢ Washington, DC 20036-4702 ♢ ph 202.331.0651 ♢ fax 202.331.0088 ♢
cirinfo@cir-safety.org

DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 4 *Saccharum officinarum* (sugarcane)-derived ingredients. These ingredients are reported to function in cosmetics as skin-conditioning agents, surfactants, exfoliants, solvents, deodorant agents, binders, skin protectants, and emulsion stabilizers. Industry should use good manufacturing practices to minimize impurities that could be present in botanical ingredients. The Panel considered the available data and concluded that… [to be determined].

INTRODUCTION

This is a safety assessment of the following 4 *Saccharum officinarum* (sugarcane)-derived ingredients as used in cosmetic formulations:

Saccharum Officinarum (Sugarcane) Bagasse Powder
Saccharum Officinarum (Sugarcane) Extract
Saccharum Officinarum (Sugarcane) Juice Extract
Saccharum Officinarum (Sugarcane) Wax

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), reported functions of these ingredients include, collectively, skin-conditioning agents, surfactants, exfoliants, solvents, deodorant agents, binders, skin protectants, and emulsion stabilizers.[1] (Table 1)

In 2019, the Expert Panel for Cosmetic Ingredient Safety (Panel) published a safety assessment on mono- and disaccharides (including sucrose, a major component of sugarcane), with the conclusion that those ingredients are safe in the present practices of use and concentration (as described in that safety assessment).[2] The full report on those ingredients can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

Botanicals, such as *Saccharum officinarum* -derived ingredients, may contain hundreds of constituents. In this assessment, the Panel is evaluating the potential toxicity of each these ingredients as a whole, complex substance; potential toxicity from exposures to mixtures of different chemical compounds may not replicate the biological activity of the individual components;

Some of the ingredients reviewed in this safety assessment may be consumed as food, and daily exposure as such would result in much larger systemic exposures than possible from use of these ingredients in cosmetic products. Therefore, although oral studies are included herein, the primary focus of this safety assessment is on the potential for local effects from topical exposure to these ingredients as used in cosmetics.

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the 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.

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard scientific practice of using italics will be followed (i.e., *Saccharum officinarum*). Often in the published literature, the general name "sugarcane" is used, and it is not known how the substance being tested compares to the cosmetic ingredient. Therefore, if it is not known that the test substance is the same as the cosmetic ingredient, the generic terminology, in all lowercase (e.g., sugarcane extract), will be used. However, if it is known that the material being tested is a cosmetic ingredient, the naming convention provided in the *Dictionary* (e.g., Saccharum Officinarum (Sugarcane) Extract) will be used.

CHEMISTRY

Definition and Plant Identification

All ingredients reviewed in this report are derived from the sugarcane plant (*Saccharum officinarum*). The definitions of the *Saccharum officinarum* (sugarcane)-derived ingredients included in this review are provided in Table 1; the generic CAS number for the majority of these ingredients is 91722-22-4.[1]

Sugarcane is a perennial grass, indigenous to tropical south and southeast Asia.[3] The plant is currently cultivated in many regions, namely Brazil and India, the largest producers of sugarcane. The plant has a thick, longitudinal stalk, which ranges from 3 - 5 m in height, and approximately 5 cm in diameter. When stalks are crushed, the remaining fibrous matter is known as bagasse.[4] The stems of the sugarcane plant vary in color (green, pink, purple), and can reach 5 cm in length. The leaves are elongated and green, with thick midribs and saw-toothed edges that grow to a length of about 30 – 60 cm, and width of 5 cm. The wax of the sugarcane plant is a whitish to dark-yellow powdery deposit on the surface of the stalks and leaves, which appears as a cuticle layer.

Chemical Properties

According to a supplier, a tradename mixture with Saccharum Officinarum (Sugarcane) Extract, prepared in glycerin and water, is a colorless to yellow liquid, with a pH ranging from 1.5 – 5.0.[5] This tradename mixture is also soluble in water, has a refractive index of 1.3920 – 1.5000 (at 25°C), and a specific gravity of 1.20 – 1.50.

Method of Manufacture

The methods described below for Saccharum Officinarum (Sugarcane) Juice Extract and Saccharum Officinarum (Sugarcane) Wax are general to the processing of these ingredients, and it is unknown if they apply to cosmetic ingredient manufacturing.

Saccharum Officinarum (Sugarcane) Extract

According to a manufacturer, sugarcane is extracted with an eluent (water, butylene glycol, glycerin, or propylene glycol) under appropriate temperature conditions, to yield a concentrate (i.e., Saccharum Officinarum (Sugarcane) Extract).[5] The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce a final tradename mixture. The tradename mixture is evaluated for chemical properties according to specification requirements. The concentrate is also evaluated for contaminants and chemical properties, as needed. In a separate study, a sugarcane extract was produced by first crushing the sugarcane (4.36 kg) and exhaustively extracting with ethyl acetate at room temperature, yielding 72 g of the crude extract.[6]

Saccharum Officinarum (Sugarcane) Juice Extract

In order to produce a sugarcane juice, the sugarcane is washed and passed through a roller mill.[7] Fresh sugarcane juice is collected in sterilized screw-capped containers and processed. The juice is then filtered by muslin cloth and pasteurized at 90 °C for five minutes. The pH of the pasteurized juice is adjusted with citric acid.

Saccharum Officinarum (Sugarcane) Wax

Press mud, which is produced during the clarification of sugarcane juice, is a source of sugarcane wax.[8] Approximately 36 - 40 kg press mud is obtained after crushing 1 ton of sugarcane. The press mud contains sugar, fiber, and coagulated colloids including cane wax, albuminoids, inorganic salts, and soil particles. In order to extract the sugarcane wax from the press mud, a Soxhlet extractor is used with different solvents, such as toluene or benzene. The extract is filtered under a mild vacuum and the solvent is removed by distillation. After removing the solvent, the solid mass containing the wax and resin is dissolved in hot isopropyl alcohol and filtered. The remaining resin is separated, and the total sugarcane wax portion obtained is yellow or light cream in color.

Composition and Impurities

Saccharum Officinarum (Sugarcane) Bagasse Powder

Crushed sugarcane stalk is composed of a sugarcane powder: cellulose (45 - 55%), hemicellulose (20 - 25%), lignin (18 - 24%), and pectin (0.6 - 0.8%), as well as extractives (1.5 - 9%).[4] Pyrolization results in 1 - 4% ash by weight.

Saccharum Officinarum (Sugarcane) Extract

Sugarcane tops were extracted with ethyl acetate (thus a *Saccharum officinarum* extract), purified, and evaluated by nuclear magnetic resonance and electrospray ionization mass spectra.[9] The phenolic compounds were identified as caffeic acid, *cis*-*p*-hydroxycinnamic acid, quercetin, apigenin, albanin A, australone A, moracin M, and 5'-geranyl-5,7,2',4'-tetrahydroxyflavone. The amount of sterols in different sugarcane extract samples was evaluated by direct saponification followed by reversed-phase-high-performance liquid chromatography (RP-HPLC).[10] Both green- and red-rind sugarcane piths, nodes, and tips were evaluated. The results exhibited that stigmasterol (varied from 883.3 ± 23.5 to 1823.9 ± 24.5 µg/g dry weight (DW)) and β-sitosterol (varied from 117.6 ± 19.9 to 801.4 ± 33.5 µg/g DW) were the major phytosterols in the sugarcane extract samples. In addition, among other parts of the sugarcane, the tips contained the greatest amount of phytosterols.

Saccharum Officinarum (Sugarcane) Juice Extract

Sugarcane juice contains 75 - 85% water, 10 - 21% sucrose, 10 - 15% fiber, 0.3 - 3% reducing sugars (glucose and fructose), and other inorganic compounds.[11] Sugarcane juice contains phytochemicals such as phenolics, sterols, terpenoids, lignins, and mixtures of long chain primary alcohols.[12] HPLC with diode-array detection (HPLC-DAD) analysis of phenolic compounds from sugarcane juice showed the presence of phenolic acids such as hydroxycinnamic acid, sinapic acid, and caffeic acids, along with flavones such as apigenin, luteolin, and tricin.[3] Among the flavones, tricin derivatives accounted for the highest concentration.

The amount of minerals and heavy metals in 12 fresh sugarcane juice samples from Multan, Pakistan was examined via furnace atomic absorption spectroscopy.[13] Mean concentrations of microelements and heavy metals were reported to be 0.352 mg/l iron, 0.129 mg/l zinc, 0.265 mg/l manganese, 0.150 mg/l copper, 0.167 mg/l lead, 0.052 cadmium, 0.085 nickel, and 0.400 mg/l cobalt.

During harvesting season, most sugarcane plantations are burnt, causing the emission of polycyclic aromatic hydrocarbons (PAHs), and thus, contamination in sugarcane products.[14] A study was performed evaluating the presence of four PAHs (benz[a]anthracene, benzo[b]fluoranthene, benzo[k]fluoranthene, and benzo[a]pyrene) in 80 samples of sugarcane juice collected from two Brazilian cities. Samples were collected in two different periods (during harvesting season and between harvests). The samples collected between harvests presented mean sums of PAHs of 0.013 µg/kg and 0.012 µg/kg, while samples collected during harvest presented mean sums of 0.053 µg/kg and 0.055 µg/kg. The most representative PAH was benzo[b]fluoranthene, which was detected in 39% of the samples.

Saccharum Officinarum (Sugarcane) Wax

The amount of wax in sugarcane plants ranges from 0.1 – 0.3%.[3] The sugarcane wax contains long chain fatty alcohols, acids, esters, aldehydes, and ketones. Aliphatic alcohols, long chain aliphatic fatty acids, steroids, and terpenoids have also been identified from sugarcane wax. Octacosanol constitutes 50 – 80% of the total aliphatic alcohols in sugarcane wax. Other such alcohols in sugarcane wax include triacontanol, hexacosanol, tetracosanol, heptacosanol, nonacosanol, dotriacontanol, and tetratriacontanol.[15]

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from the US Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics. Use frequencies of individual ingredients in cosmetics are collected from manufacturers and reported by cosmetic product category in the FDA Voluntary Cosmetic Registration Program (VCRP) database. Use concentration data are submitted by the cosmetic industry in response to a survey, conducted by the Personal Care Products Council (Council), of maximum reported use concentrations by product category.

According to 2021 VCRP survey data, Saccharum Officinarum (Sugarcane) Extract is reported to be used in 211 formulations (121 of which are leave-on formulations; Table 2).[16] The results of concentration of use surveys conducted by the Council in 2019[17] and 2020[18] indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use in leave-on formulations; it is used at up to 2.4% in foot powders and sprays.[17] Use concentration data were reported for Saccharum Officinarum (Sugarcane) Wax (up to 0.012% in skin cleansing products)[17] and Saccharum Officinarum (Sugarcane) Juice Extract (up to 0.26% in skin cleansing products),[18] but no uses were reported in the VCRP; it should be presumed there is at least one use for the category in which the concentration is reported. No uses were reported for Saccharum Officinarum (Sugarcane) Bagasse Powder.

Saccharum Officinarum (Sugarcane) Extract is reported to be used in products that may result in incidental eye or mucous membrane exposure. For example, this ingredient is reported to be used in eye lotions (no concentration reported) and bath soaps and detergents (at up to 0.00093%).

Additionally, Saccharum Officinarum (Sugarcane) Extract is used in cosmetic sprays and could possibly be inhaled; for example, this ingredient is reported to be used hair sprays (at up to 0.023%) and spray body and hand products (at up to 0.12%). In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[19,20] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[21,22] Additionally, Saccharum Officinarum (Sugarcane) Extract is reported to be used in foot powders and sprays at concentrations up to 2.4%. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the air.[23-25]

None of the sugarcane ingredients named in the report are restricted from use in any way under the rules governing cosmetic products in the European Union.[26]

Non-Cosmetic

Sugarcane juice is the first material used for the production of table sugar and other various products, such as raw sugar/brown sugar, jaggery (traditional, concentrated sugarcane juice), and molasses.[3,27] In some regions, the sugarcane is chewed raw, or crushed, and the resulting fresh juice is consumed.[13,28] In addition, chopped sugarcane stalks and tops are reported to be used as cattle feed.[29]

Sugarcane juice is used in holistic medicine.[11] In Indian Ayurveda, sugarcane juice is used as a diuretic, for hiccup relief, laxative, coolant, demulcent, and antiseptic. Sugarcane juice has also been recommended in ayurvedic medicine for patients suffering from low blood pressure, gastrointestinal issues, and jaundice. In Cambodia, sugarcane juice is an integral component of medicines used to treat ulcers of the skin and mucous membranes. Aliphatic alcohols and long chain aliphatic fatty acids, commonly isolated from sugarcane wax, are pharmacologically active substances used for their anti-inflammatory, anti-hypercholesterolemic, and anti-thrombotic effects.[3]

Sugarcane bagasse is used as a fuel source in sugarcane mill furnaces.[4] Other industrial purposes for bagasse includes alcohol production and papermaking.[4]

TOXICOKINETIC STUDIES

Toxicokinetics studies were not found in the published literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Oral

Saccharum Officinarum (Sugarcane) Juice Extract

Adult male Wistar rats (1 rat/group) were given 1600, 2900, or 5000 mg/kg sugarcane juice via gavage.[30] Animals were observed for 24 h. No deaths were observed; therefore, the LD_{50} of the test substance was considered to be greater than 5000 mg/kg.

Saccharum Officinarum (Sugarcane) Wax

The acute oral toxicity potential of a mixture of higher aliphatic primary acids purified from *Saccharum officinarum* wax was evaluated in Wistar rats (3 rats/sex/group).[31] Animals were dosed with this mixture suspended in acacia gum and distilled water (10 mg/ml water), via gastric gavage, in doses of either 50, 20, or 2000 mg/kg. Control animals were given similar volumes of acacia gum-water by the same route. No deaths occurred during the study, and clinical observations did not show evidence of test substance-related toxicity. No gross histopathological alterations were found at necropsy.

Subchronic and Chronic Toxicity Studies

Details of the subchronic and chronic oral toxicity studies summarized below are described in Table 3.

A 90-d oral toxicity assay was performed using Sprague-Dawley rats (3 animals/sex/group).[31] Animals were dosed with a mixture of higher aliphatic primary acids purified from sugarcane wax suspended in acacia gum and distilled water, via gastric gavage, in doses of up to 1250 mg/kg/d. No hematological or clinical signs of toxicity attributable to the test substance were observed.

The potential oral toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in Sprague-Dawley rats (20 rats/sex/group) for 6 mo.[32] Each group was given this mixture suspended in acacia gum in distilled water via gavage at doses of up to 1000 mg/kg/d. A control group was given the vehicle only (acacia gum/water). All evaluated parameters were similar between control and treated groups. A similar long-term toxicity study was performed in Sprague-Dawley rats (60/sex/group).[33] Animals were given up to 1500 mg/kg of a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum water via gavage, 5 d/wk, for 24 mo. A control group was treated with the vehicle only. Signs of toxicity were evaluated. (Carcinogenicity results from this study can be found in the Carcinogenicity section of this report.) Serum cholesterol levels in groups treated with 500 and 1500 mg/kg this mixture were lower than controls. All other toxicity results were similar among control and treated groups.

Beagle dogs (4 animals/sex/group) were used in a 1-yr study evaluating the potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax (30 or 180 mg/kg/d via gavage).[15] No clinical, hematological, or histopathological evidence of toxicity were observed throughout the study; however, lipid profile determinations showed that treatment with 30 or 180 mg/kg/d of this mixture decreased total cholesterol by 20% on wk 8 to 52 of treatment. The potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax was also evaluated in male *Macaca artoides* monkeys (6 animals/ group).[34] This mixture (up to 25 mg/kg/d), was fed to the monkeys once a day, for 54 wk. No signs of toxicity were observed; however, a significant reduction in serum total cholesterol and low-density lipoprotein cholesterol was observed in alcohol mixture-treated animals when compared with controls.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Details of the oral DART studies summarized below are described in Table 4.

Saccharum Officinarum (Sugarcane) Wax

A sperm morphology assay was performed in CEN/NMRI mice (8 animals/group).[35] Mice were treated with a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gavage at 5, 50, or 500 mg/kg/d for 90 d, and sacrificed 24 h after the last administration. A control group received the vehicle only. Results were similar in both the control and treated groups. In a study involving rats, pregnant Sprague-Dawley rats (25 rats/group) were given a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum solution via gavage at up to 1000 mg/kg/d.[36] Administration occurred on days 6 - 15 of gestation. No signs of maternal or developmental toxicity were observed.

Similarly, no signs of maternal or fetal toxicity were observed in a different study in which pregnant Sprague-Dawley rats (25 rats/group) were given the same test substance via gavage on day 15 of pregnancy, through gestation, until day 21 post-partum.[37] The potential reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in both male and female Sprague-Dawley rats (30 females and 15 males/group).[38] Females were treated via gavage with 500 or 1000 mg/kg/d before mating, through mating and gestation, to day 21 of lactation. Males were treated with the same doses for 4 wk before and during mating. No signs of developmental or reproductive toxicity were observed. The reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in New Zealand White rabbits (27 females/group). Pregnant rabbits were given this mixture in an acacia gum solution at doses of either 500 or 1000 mg/kg/d on days 6 - 18 of gestation. Administration occurred via gavage. A control group consisting of 27 pregnant female rabbits were given the vehicle only. No evidence of embryotoxicity or teratogenicity was observed.

GENOTOXICITY STUDIES

In Vivo

Saccharum Officinarum (Sugarcane) Wax

A bone marrow micronucleus test was performed in CEN/NMRI mice (6 - 8 animals/sex/group).[35] Animals were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gastric gavage at 5, 50, or 500 mg/kg for 90 d, and sacrificed 24 h after the last administration. Control animals were given the vehicle only. The test substance did not increase the frequency of micronucleated polychromatic erythrocytes, nor the ratio of polychromatic to normochromatic erythrocytes, compared with the controls. (Results regarding sperm morphology can be seen in the DART section of this report.) In a second series of the same study, a micronucleus assay was performed in CEN/NMRI mice of both sexes given 2000 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water via gastric gavage for 6 d. No genotoxic effects were observed.

An alkaline comet assay was performed with five male Sprague-Dawley rats.[35] Animals were treated with the vehicle (acacia gum/water) or with a mixture of higher aliphatic primary acids purified from sugarcane wax at 1250 mg/kg via gavage for 90 d. Positive control groups were treated with an injection of 50 mg/kg cyclophosphamide. Sampling time was 24 h after the last administration for all groups, and responses of rat liver cells to the test substance were assessed. No single-strand breaks or alkali-labile site induction on DNA was observed.

CARCINOGENICITY STUDIES

Saccharum Officinarum (Sugarcane) Wax

The carcinogenic potential of a mixture of long-chain primary alcohols purified from sugarcane wax was evaluated for carcinogenicity in male and female Swiss mice (80 animals/sex/ group).[39] Animals were administered the test substance (50 mg/kg or 500 mg/kg of this mixture in acacia gum and water) at a volume of 5 ml/kg, daily, via gavage, for 18 mo. Control mice were given similar volumes of acacia gum and water. The frequency of neoplastic lesions was similar in control and treated groups. Since no treatment-related increased in the occurrence of malignant of benign neoplasms were found, nor acceleration in tumor growth in any specific group observed, the test substance was considered to be non-carcinogenic in Swiss mice.

In a different study, a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in OF1 mice (50 mice/sex/group).[40] This mixture, in a vehicle of acacia gum and water, was administered to mice via gavage at doses of 50, 500, or 1500 mg/kg. Treatments were given 6 d/wk, for 18 mo. A control group was treated with the vehicle only. The test substance did not increase the frequency of neoplastic or non-neoplastic lesions with respect to controls. Lesions observed in this study were consistent with spontaneous lesions reported for this species.

A similar study was performed using Sprague Dawley rats (60/sex/group).[33] Animals were given either 50, 500, or 1500 mg/kg a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum water via gavage, 5 d/wk, for 24 mo. A control group was treated with the vehicle only. Mortality, clinical symptoms, weight gain, food consumption, organ weight, and tumor incidence were evaluated. (Toxicity results can be found in the Chronic Toxicity section of this report.) The frequency of neoplastic and non-neoplastic lesions was similar in control and treated groups. The occurrence of mammary tumors in females treated with this mixture was lower than in controls. The test substance was considered to be non-carcinogenic.

ANTI-CARCINOGENICITY STUDIES

In Vitro

Saccharum Officinarum (Sugarcane) Extract

The cytotoxic activity of a sugarcane extract (0.25 - 250 µg/ml; ethyl acetate) against 8 human tumor cell lines (U251 (glioma), MCF-7 (breast), NCI-ADR/RES (multiple drug-resistant ovary cells), 786-0 (kidney), NCI-H460 (lung, non-small

cells), PC-3 (prostate), OVCAR-03 (ovary), and HT29 (colon)), was evaluated.[6] In general, the ethyl acetate extract showed cytostatic activity in the human tumor cell lines in concentrations ranging from 25.8 to 61.8 µg/ml.

OTHER RELEVANT STUDIES

Sensitization to Sugarcane Pollen in Children

Specific immunoglobin E (IgE) antibodies to sugarcane pollen were investigated by a radioallergosorbent test (RAST) in 74 children from Okinawa, Japan who suffer from allergic disorders.[41] Forty-seven of the patients were found to have asthma, 8 had atopic dermatitis, 9 had asthma and atopic dermatitis, 6 had asthma and allergic rhinitis, and 4 had atopic dermatitis and allergic rhinitis. The mean of the serum IgE levels for the group was 962.6 ± 1237.1 IU/ml. RAST results were scored by comparison to serially diluted reference sera from patients with sensitivity to pollen of *Betula platyphylla*. RAST scores of 2+, 3+, and 4+ were considered positive. Of all the patients tested, only 2 reacted to sugarcane pollen, both being asthmatic patients.

Allergic Potential of Airborne Sugarcane Pollen

The potential allergenic effect of airborne pollen grains of different plant species was evaluated in West Bengal, India.[42] When performing a 2-yr volumetric aerobiological survey, 31 pollen types were identified, and sugarcane pollen showed maximum frequency. Clinical investigations by skin prick tests were carried out to detect the allergenic potential of the crude pollen extracts. Patients (n = 350) with respiratory disorders were evaluated. Ninety percent pure pollen was defatted with diethyl ether and extracted in sodium phosphate buffer. Wheal responses to the test substance (20 ml sugarcane pollen extract) were evaluated 20 min after skin prick test, and graded on a scale of 1+ to 3+. A positive control of 1 mg/ml histamine diphosphate was used. Fifty-four percent of patients elicited a positive response to the sugarcane pollen extract, while 15% of patients had a reaction rated a 2+ or more.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Human

Saccharum Officinarum (Sugarcane) Extract

The cutaneous tolerance of a rinse-off face mask formulation containing 0.36% Saccharum Officinarum (Sugarcane) Extract was evaluated in 21 subjects.[43] The undiluted product was applied to the skin, left on for 10 min, and rinsed off, twice a week, for 21 d. Irritation parameters were measured before and after 21 d of treatment. The product was considered to be very well-tolerated.

Sensitization

Human

Saccharum Officinarum (Sugarcane) Extract

A human repeat insult patch test (HRIPT) was performed on 105 subjects using a facial serum containing 1.44% Saccharum Officinarum (Sugarcane) Extract.[44] The test substance was applied neat and under an occlusive patch during induction and challenge phases. No other details regarding study methods were provided. The test substance was considered to be non-irritating and non-sensitizing.

An HRIPT was also performed using a facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract.[45] Approximately 0.2 g of the undiluted moisturizer was applied to the skin of the subjects (n = 105), under a semi-occlusive patch, 3 times/wk, for 3 wk; test sites were evaluated prior to re-application. The duration of each application and patch size was not noted. After a 2-wk non-treatment period, the same test substance was applied to a previously untreated site under semi-occlusive conditions. Challenge sites were evaluated 24 and 72 h post-application. The test substance was considered to be non-irritating and non-sensitizing.

OCULAR IRRITATION STUDIES

No ocular irritation studies were found in the published literature, and unpublished data were not submitted.

SUMMARY

The safety of 4 *Saccharum officinarum* (sugarcane)-derived ingredients as used in cosmetics is reviewed in this safety assessment. All ingredients reviewed in this report are derived from the sugarcane plant. According to the *Dictionary*, collectively, these ingredients are reported to function as skin-conditioning agents, surfactants, exfoliants, solvents, deodorant agents, binders, and skin protectants, in cosmetic products.

According to 2021 VCRP data, the ingredient with the most reported uses is Saccharum Officinarum (Sugarcane) Extract, which is reported to be used 211 formulations (121 of which are leave-on formulations). The results of concentration of use surveys conducted by the Council indicate Saccharum Officinarum (Sugarcane) Extract also has the highest concentration of use; it is used at up to 2.4% in foot powders and sprays.

An oral LD_{50} of greater than 5000 mg/kg was determined in an acute toxicity assay involving Wistar rats given up to 5000 mg/kg sugarcane juice via gavage. The acute toxicity potential of a mixture of higher aliphatic primary acids purified from sugarcane wax was evaluated in Wistar rats. Animals were given this mixture in acacia gum and water via gavage at doses of up to 2000 mg/kg. No deaths or signs of toxicity were observed.

No hematological or clinical signs of toxicity were observed when Sprague-Dawley rats were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum and water (up to 1250 mg/kg/d), via gavage, for 90 d. The same test substance was also evaluated in Sprague-Dawley rats for 6 mo. The test substance was given via gavage at doses of up to 1000 mg/kg/d. All evaluated parameters were similar between control and treated groups. A similar long-term toxicity assay was performed on Sprague-Dawley rats using a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum and water (up to 1500 mg/kg/d), via gavage, for 24 mo. Serum cholesterol levels in groups treated with 500 and 1500 mg/kg of this mixture were lower than controls. All other toxicity results were similar among control and treated groups. The chronic toxicity of a mixture of long-chain primary alcohols purified from sugarcane wax was studied in beagle dogs. A mixture of higher aliphatic primary acids purified from sugarcane wax, in a vehicle of acacia gum and water, was given to the animals, via gavage, in doses of either 30 or 180 mg/kg/d, for 1 yr. No signs of toxicity were observed; treatment with the test substance resulted in a decrease in total cholesterols on wk 8 to 52 of treatment. The potential toxicity of a mixture of long-chain primary alcohols purified from sugarcane was also evaluated in male *Macaca artoides* monkeys. The test substance was fed to the monkeys, wrapped in banana, for 54 wk. No signs of toxicity were observed; however, a significant reduction in serum total cholesterol and low-density lipoprotein cholesterol was observed in treated animals compared to controls.

A sperm morphology assay on a mixture of higher aliphatic primary acids purified from sugarcane wax was performed in CEN/NMRI mice. This mixture in acacia gum and water was given to the animals at doses of up to 500 mg/kg/d, for 90 d. A control group was given the vehicle only. Results were similar in the control and treated groups. In a different study, pregnant Sprague-Dawley rats were given a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum solution (up to 1000 mg/kg/d), via gavage, on days 6 - 15 of gestation. No signs of developmental or maternal toxicity were observed. Similarly, no signs of maternal or fetal toxicity were observed in a different study in which female Sprague-Dawley rats were given the same test substance, on day 15 of pregnancy, until day 21 post-partum. The potential reproductive toxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax was also evaluated in both male and female Sprague-Dawley rats. Females were treated via gavage with up to 1000 mg/kg/d before mating, through mating and gestation, to day 21 of lactation. Male rats were treated for 4 wk, before and during mating. No signs of developmental or reproductive toxicity were observed. In a different study, pregnant New Zealand White rabbits were given a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum solution at doses of up to 1000 mg/kg/d, via gavage, on days 6 - 18 of gestation. No evidence of embryotoxicity or teratogenicity was observed.

The potential genotoxicity of a mixture of higher aliphatic primary acids purified from sugarcane wax in acacia gum/water was evaluated in CEN/NMRI mice. Animals were given the test substance, at doses of up to 500 mg/kg, for 90 d. The test substance did not increase the frequency of micronucleated polychromatic erythrocytes, nor the ratio of polychromatic to normochromatic erythrocytes, compared with the controls. In a second series of the same study, a micronucleus assay was performed in CEN/NMRI mice of both sexes given 2000 mg/kg of this mixture in acacia gum/water via gastric gavage for 6 d. No genotoxic effects were observed. An alkaline comet assay was performed using five male Sprague-Dawley rats. Rats were treated with a mixture of higher aliphatic primary acids purified from sugarcane wax in an acacia gum/water vehicle (1250 mg/kg) for 90 d. No single-strand breaks or alkali-labile site induction on DNA was observed.

In a carcinogenicity assay, no signs of carcinogenicity were observed in an assay involving Swiss mice. Animals were administered up to 500 mg/kg of the test substance (a mixture of long-chain primary alcohols purified from sugarcane wax in acacia gum and water), via gavage, for 18 mo. Similarly, a mixture of higher aliphatic primary acids purified from sugarcane wax, in acacia gum and water, was administered to OF1 mice, via gavage, at doses of up to 1500 mg/kg. Treatment lasted for 18 mo. The test substance did not increase the frequency of neoplastic or non-neoplastic lesions with respect to controls. A similar study was performed using the same test substance and concentrations in Sprague-Dawley rats. Animals were treated via gavage for 24 mo. The test substance was considered to be non-carcinogenic.

The cytotoxic potential of a sugarcane extract (0.25 - 250 µg/ml; ethyl acetate) against 8 human cancer cell lines was evaluated in an in vitro assay. In general, the ethyl acetate extract showed cytostatic activity in the human tumor cell lines in concentrations ranging from 25.8 to 61.8 µg/ml.

Specific IgE antibodies to sugarcane pollen were investigated using a RAST in 74 children from Okinawa, Japan who suffer from allergic disorders. Of all the patients tested, only 2 reacted to sugarcane pollen, both being asthmatic patients. In a different study, the potential allergic effect of airborne pollen grains of different plant species was evaluated in West

Bengal, India. Clinical investigations by skin prick tests were carried out to determine the allergenic potential of these crude pollen extracts, including a crude sugarcane pollen extract. Fifty-four percent of patients (n = 350) elicited a positive response to the sugarcane pollen extract, while 15% of patients had a reaction rated a 2+ or more.

A rinse-off face mask formulation containing 0.36% Saccharum Officinarum Extract was considered to be well-tolerated on a cutaneous level, in 21 subjects, in a 21-d irritation assay. A facial serum containing 1.44% Saccharum Officinarum (Sugarcane) Extract and a facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract were considered to be non-irritating and non-sensitizing when evaluated using HRIPTs; both studies were completed in 105 subjects.

DRAFT DISCUSSION

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

This assessment reviews the safety of 4 *Saccharum officinarum* (sugarcane)-derived ingredients, as used in cosmetic formulations. The Panel concluded [TBD].

The Panel noted that elevated levels of heavy metals and pesticide residues may be present in these sugarcane-derived ingredients. The Panel also expressed concern regarding potential PAH contamination following sugarcane plantation burning during harvesting season. The cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit these PAH impurities, as well as heavy metal and pesticide residues.

The need for systemic toxicity and sensitization/irritation data on Saccharum Officinarum (Sugarcane) Wax was mitigated due to low concentrations of use in rinse-off formulations only. In addition, because Saccharum Officinarum (Sugarcane) Wax is predominantly composed of long-chain fatty alcohols and acids, little to no dermal absorption would be expected, further mitigating the need for systemic toxicity data on this ingredient.

The Panel discussed the issue of incidental inhalation exposure resulting from these ingredients (e.g., Saccharum Officinarum (Sugarcane) Extract is used at up to 0.12% in spray body and hand formulations and up to 2.4% in foot powders and sprays). Inhalation toxicity data were not available. However, the Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

CONCLUSION

To be determined.

TABLES

Table 1. INCI names, definitions, and functions of the *Saccharum officinarum* (sugarcane)-derived ingredients in this safety assessment[1]

Ingredient (CAS No.)	Definition	Function
Saccharum Officinarum (Sugarcane) Bagasse Powder	Saccharum Officinarum (Sugarcane) Bagasse Powder is the powder obtained from the dried, ground residue, or bagasse, from the stalks of *Saccharum officinarum* after the juice has been removed.	skin-conditioning agents – humectant; surfactants – cleansing agents
Saccharum Officinarum (Sugarcane) Extract (91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Extract is the extract of the sugarcane, *Saccharum officinarum*	exfoliants; skin-conditioning agents – miscellaneous; solvents
Saccharum Officinarum (Sugarcane) Juice Extract (91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Juice Extract is the extract of the juice of the sugarcane, *Saccharum officinarum*	deodorant agents; skin-conditioning agents – miscellaneous
Saccharum Officinarum (Sugarcane) Wax (142583-61-7; 91722-22-4 [generic])	Saccharum Officinarum (Sugarcane) Wax is the wax obtained from *Saccharum officinarum*	binders; emulsion stabilizers; skin protectants

Table 2. Frequency (2021) and concentration (2019; 2020) of use of *Saccharum officinarum* (sugarcane)-derived ingredients[16-18]

	# of Uses[16]	Conc of Use (%)[17]	# of Uses[16]	Conc of Use (%)[18]	# of Uses[16]	Conc of Use (%)[17]
	Saccharum Officinarum (Sugarcane) Extract		Saccharum Officinarum (Sugarcane) Juice Extract		Saccharum Officinarum (Sugarcane) Wax	
Totals*	**211**	**0.00024 – 2.4**	**NR**	**0.0009 – 0.26**	**NR**	**0.0012**
Duration of Use						
Leave-On	*121*	*0.00024 – 2.4*	*NR*	*0.0009 – 0.001*	*NR*	*NR*
Rinse-Off	*90*	*0.00024 – 0.5*	*NR*	*0.001 – 0.26*	*NR*	*0.0012*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	1	0.0075	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	49[a]; 22[b]	0.0019 – 0.12; 2.4[a]; 0.0024 – 0.25[b]	NR	NR	NR	NR
Incidental Inhalation-Powder	49[a]	2.4[a]; 0.036[c]	NR	NR	NR	NR
Dermal Contact	173	0.00024 – 2.4	NR	0.0009 – 0.26	NR	0.0012
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	36	0.00024 – 0.25	NR	0.001	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	2	NR	NR	NR	NR	NR
Mucous Membrane	33	0.00093	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR

	# of Uses[16]	Conc of Use (%)
	Saccharum Officinarum (Sugarcane)[d]	
Totals*	**4**	**NS**
Duration of Use		
Leave-On	*4*	*NS*
Rinse-Off	*NR*	*NS*
Diluted for (Bath) Use	*NR*	*NS*
Exposure Type		
Eye Area	NR	NS
Incidental Ingestion	NR	NS
Incidental Inhalation-Spray	1[a]; 1[b]	NS
Incidental Inhalation-Powder	1[a]	NS
Dermal Contact	4	NS
Deodorant (underarm)	NR	NS
Hair - Non-Coloring	NR	NS
Hair-Coloring	NR	NS
Nail	NR	NS
Mucous Membrane	NR	NS
Baby Products	NR	NS

*Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.
[a] Not specified that these products or 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
[b] It is possible these products are sprays, but it is not specified whether the reported uses are sprays.
[c] It is possible these products are powders, but it is not specified whether the reported uses are powders
[d] Reported in the VCRP under a non-INCI name and presented here for informational purposes
NR – no reported use
NS – not surveyed

Table 3. Repeated dose oral toxicity studies

Test Substance	Animals/Group	Study Duration	Vehicle/Method	Dose	Results	Reference
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (3 rats/sex)	90 d	Acacia gum and distilled water; gavage	0, 50, 500, 1250 mg/kg/d	One death was observed, corresponding to a female rat treated with 500 mg/kg, who died 9 d after treatment. The death was considered to be related to gastric gavage manipulation. No signs of clinical toxicity attributable to the test substance were observed throughout the study. No signs of toxicity were observed based on hematological or necropsy results.	[31]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (20 rats/sex)	6 mo	Acacia gum and distilled water; gavage	0, 250, 500, or 1000 mg/kg/d	Body weight gain, food consumption, clinical observations, blood biochemistry, hematology, organ weight ratios and histopathological findings were similar between control and treated groups.	[32]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (60 rats/sex)	24 mo	Acacia gum and water; gavage; administration 5 d/wk	0, 50, 500, or 1500 mg/kg/d	Toxicity results relating to mortality, clinical symptoms, weight gain, food consumption, and organ weight were similar among control and treated groups. However, serum cholesterol levels in groups treated with 500 and 1500 mg/kg were lower than in controls. No other differences in blood indicators were found.	[33]
a mixture of long-chain primary alcohols purified from sugarcane wax	Beagle dogs (4 dogs/sex)	12 mo	Acacia gum and water; by gavage	30 or 180 mg/kg/d	No signs of toxicity were observed throughout the study. Lipid profile determinations showed that a mixture of long-chain primary alcohols purified from sugarcane wax decreased total cholesterol by 20% from wk 8 to 52 of treatment. No hematological or histopathological disturbances attributable to treatment were observed.	[15]
a mixture of long-chain primary alcohols purified from sugarcane wax	Male *Macaca artoides* monkeys (6 male monkeys)	54 wk	Test substance was fed wrapped in a piece of banana	0, 0.25, 2.5, or 25 mg/kg/d	No signs of toxicity were observed when behavior, physical condition, hematological parameters, or blood biochemistry were evaluated. In addition, no adverse effects were observed when ophthalmological and pathological anatomy examinations were performed at the end of the administration period. After 8 wk, a significant reduction of serum total cholesterol and low-density lipoprotein cholesterol was observed in treated animals when compared with controls. This effect persisted throughout the study.	[34]

Table 4. Oral developmental and reproductive toxicity studies

Test Article	Animals/Group	Vehicle	Dose	Procedure	Results	Reference
a mixture of higher aliphatic primary acids purified from sugarcane wax	CEN/NMRI mice (8 males)	Acacia gum and water	0, 5, 50, and 500 mg/kg/d	Mice were treated via gavage for 90 d and killed 24 h after the last administration. Control animals were given the vehicle only.	The test substance did not change the sperm count or frequency of all types of abnormal head shapes, compared with controls.	[35]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley Rats (25 females)	Acacia gum and water	0, 5, 100, and 1000 mg/kg/d	Pregnant rats were given the test substance by gavage on days 6 through 15 of gestation. Cyclophosphamide (50 mg/kg/d) was given as a positive control. Negative control animals were given the vehicle only.	No adverse effects on reproductive performance, or on embryonic or fetal development, were seen in any of the groups treated with a mixture of higher aliphatic primary acids purified from sugarcane wax. No signs of developmental toxicity were observed in treated groups. No signs of maternal toxicity were observed, and body weight gain during treatment period was comparable among treated and negative control rats. The positive control caused embryotoxic and teratogenic effects.	[36]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (25 females)	Acacia gum and water	0, 500 or 1000 mg/kg/d	Pregnant females received the test substance via gavage on day 15 of pregnancy, through gestation, until day 21 post-partum. A control group was given the vehicle only. Dams and F1 pups were evaluated for signs of toxicity.	No spontaneous or dose-related maternal deaths were reported during the study. The general health and condition of offspring was good in treated and control groups. No significant differences between treated and control groups were reported regarding litter size, survival through the weaning period, sex ratio, and pup weight.	[37]
a mixture of higher aliphatic primary acids purified from sugarcane wax	Sprague-Dawley rats (30 females and 15 males)	Acacia gum and water	0, 500 or 1000 mg/kg/d	The test substance was given via gavage to female rats for 15 d prior to mating, through mating and gestation, to day 21 of lactation. Male rats were treated for 4 wk prior to and during mating. A control group of 15 males and 30 females was given the vehicle only. Effects on growth, development, reproductive performance, and fertility of the F1 generation were assessed.	There were no significant reductions in the number of animals that conceived, in the number of pups born to those that did conceive, in the number of pups that survived until weaning, or body weights of pups at weaning. Control and treated group offspring were comparable in growth, physical and behavioral development, and reproductive performance. The NOAEL was considered to be 1000 mg/kg/d.	[38]
a mixture of higher aliphatic primary acids purified from sugarcane wax	New Zealand White rabbits (27 females)	Acacia gum and water	0, 500 or 1000 mg/kg/d	Mated females were given the test substance via gavage on gestation days 6-18. An additional control group of 27 mated females was given the vehicle only. All animals were euthanized on gestation day 29, the corpora lutea were counted, the location and number of implantation sites were recorded, and all fetuses were weighed, sexed, and examined.	No evidence of embryotoxicity or teratogenicity was observed. The NOAEL was considered to be 1000 mg/kg/d.	[38]

REFERENCES

1. Nikitakis J, Kowcz A. wINCI: *International Cosmetic Ingredient Dictionary and Handbook.* http://webdictionary.personalcarecouncil.org/jsp/Home.jsp. Washington, DC: Personal Care Products Council. Last Updated: 2020. Accessed: March 10, 2020.

2. Fiume M, Bergfeld W, Belsito D, et al. Safety Assessment of Monosaccharides, Disaccharides, and Related Ingredients as Used in Cosmetics. *Int J Toxicol.* 2019;38(1 Suppl):5S-38S.

3. Singh A, Lal UR, Mukhtar HM, Singh PS, Shah G, Dhawan RK. Phytochemical profile of sugarcane and its potential health aspects. *Pharmacogn Rev.* 2015;9(17):45-54.

4. Yadav S, Gupta G, Bhatnagar R. A review on composition and properties of bagasse fibers. *IJSER.* 2015;6(5):143-148.

5. Anonymous. 2020. Saccharum Officinarum (Sugarcane) Extract. (Unpublished data submitted by Personal Care Products Council on October 1, 2020)

6. Alves VG, Souza AG, Chiavelli LU, et al. Phenolic compounds and anticancer activity of commercial sugarcane cultivated in Brazil. *An Acad Bras Cienc.* 2016;88(3):1201-1209.

7. Yasmin A, Masood S, Abid H. Biochemical analysis and sensory evaluation of naturally preserved sugarcane juice. *Pak J Biochem Mol Biol.* 2010;43(3):144-145.

8. Chonde S, Bhosale P, Raut PD. Studies on extraction of sugarcane wax from press mud of sugar factories from Kolhapur district, Maharashtra. *JERAD.* 2012;6(3A):715-720.

9. Sun J, He XM, Zhao MM, Li L, Li CB, Dong Y. Antioxidant and nitrite-scavenging capacities of phenolic compounds from sugarcane (*Saccharum officinarum L.*) tops. *Molecules.* 2014;19(9):13147-13160.

10. Feng S, Liu S, Luo Z, Tang K. Direct saponification in preparation and analysis of free and conjugated phytosterols in sugarcane (*Saccharum officinarum L.*) by reversed-phase high-performance liquid chromatography. *Food Chem.* 2015;181:9-14.

11. Nisha M, Chandran K, Gopi R, Krishnapriya V, Mahendran B. Nutritional and therapeutic benefits of sugarcane and it's products. *Journal of Sugarcane Research.* 2017;7(1):1-10.

12. Ali SE, El Gedaily RA, Mocan A, Farag MA, El-Seedi HR. Profiling Metabolites and Biological Activities of Sugarcane (*Saccharum officinarum Linn.*) Juice and its Product Molasses via a Multiplex Metabolomics Approach. *Molecules.* 2019;24(5):934.

13. Akhtar S, Ismail T, Riaz M. Safety assessment of street vended juices in Multan-Pakistan: A Study on prevalence levels of trace elements. *IJFAAS.* 2015;1(1):1-10.

14. Silvia AV, Natali GS, Milton BN. Polycyclic aromatic hydrocarbons in sugarcane juice. *Food Chem.* 2009;116(1):391-394.

15. Mesa AR, Mas R, Noa M, et al. Toxicity of policosanol in beagle dogs: one-year study. *Toxicol Lett.* 1994;73(2):81-90.

16. U.S. Food and Drug Administration Center for Food Safety & Applied Nutrition (CFSAN). 2021. Voluntary Cosmetic Registration Program - Frequency of Use of Cosmetic Ingredients. Obtained under the Freedom of Information Act from CFSAN; requested as "Frequency of Use Data" January 4, 2021; received January 21, 2021. College Park, MD.

17. Personal Care Products Council. 2019. Concentration of Use by FDA Product Category: Saccharum Officinarum (Sugarcane) Extract, Saccharum Officinarum (Sugarcane) Wax. (Unpublished data submitted to Personal Care Products Council on July 24, 2019.)

18. Personal Care Products Council. 2020. Concentration of Use by FDA Product Category: Sugarcane Additions (Saccharum Officinarum (Sugarcane) Juice Extract, Saccharum (Officinarum) Bagasse Powder) (Unpublished data submitted by Personal Care Products Council on October 7, 2020.)

19. Johnsen M. The influence of particle size. *Spray Technol Marketing.* 2004;14(11):24-27.

20. Rothe H. Special Aspects of Cosmetic Spray Evaluation. 2011. Unpublished data presented at the 26 September 2011 Expert Panel meeting. Washington, D.C.

21. Bremmer HJ, Prud'homme de Lodder L, van Engelen J. Cosmetics Fact Sheet: To assess the risks for the consumer, Updated version for ConsExpo4. Bilthoven, Netherlands. 2006. http://www.rivm.nl/bibliotheek/rapporten/320104001.pdf. Accessed June 25, 2019. Pages 1-77.

22. Rothe H, Fautz R, Gerber, E, et al. Special aspects of cosmetic spray safety evaluations: Principles on inhalation risk assessment. Netherlands National Institute for Public Health and Environment; Bilthoven, Netherlands. *Toxicol Lett.* 2011;205(2):97-104.

23. CIR Science and Support Committee of the Personal Care Products Council (CIR SCC). 2015. (Nov 3rd) Cosmetic Powder Exposure. Unpublished data submitted by the Personal Care Products Council.

24. Aylott R, Byrne G, Middleton J, Roberts M. Normal use levels of respirable cosmetic talc: preliminary study. *Int J Cosmet Sci.* 1979;1(3):177-186.

25. Russell R, Merz R, Sherman W, Siverston J. The determination of respirable particles in talcum powder. *Food Cosmet Toxicol.* 1979;17(2):117-122.

26. European Commission. CosIng database; following Cosmetic Regulation No. 1223/2009. http://ec.europa.eu/growth/tools-databases/cosing/. Last Updated: 2016. Accessed: 03/10/2020.

27. Sahu AP, Saxena AK. Enhanced translocation of particles from lungs by jaggery. *Environ Health Perspect.* 1994;102:211-214.

28. Abbas SR, Sabir SM, Ahmad SD, Boligon AA, Athayde ML. Phenolic profile, antioxidant potential and DNA damage protecting activity of sugarcane (*Saccharum officinarum*). *Food Chem.* 2014;147:10-16.

29. Kawashima T, Sumamal W, Pholsen P, Chaithiang R. The use of sugarcane stalk for feeding lactating cows. *AJAS.* 2002;15(2):205-208.

30. Karaye RM, Dikko AAU, Yarube IU, et al. Effect of sugarcane juice on lipid profile, liver enzymes, and sex hormones in male Wistar rats. *Bayero Journal of Medical Laboratory Sciences.* 2017;7(2):74-79.

31. Gamez R, Mas R, Noa M, et al. Acute and oral subchronic toxicity of D-003 in rats. *Toxicol Lett.* 2000;118(1-2):31-41.

32. Gamez R, Mas R, Noa M, et al. Six-month toxicity study of oral administration of D-003 in Sprague Dawley rats. *Drugs in R&D.* 2002;3(6):375-386.

33. Gamez R, Noa M, Mas R, et al. Long-term carcinogenicity of D-003, a mixture of high molecular weight acids from sugarcane wax, in Sprague Dawley rats: a 24 months study. *Food Chem Toxicol.* 2007;45(12):2352-2358.

34. Rodriguez-Echenique C, Mesa R, Mas R, et al. Effects of policosanol chronically administered in male monkeys (*Macaca arctoides*). *Food Chem Toxicol.* 1994;32(6):565-575.

35. Gamez R, Gonzalez JE, Rodeiro I, et al. In Vivo Genotoxic Evaluation of D-003, a Mixture of Very Long Chain Aliphatic Acids. *J Med Food.* 2001;4(2):85-91.

36. Rodriguez MD, Gamez R, Gonzalez JE, Garcia H, Acosta CP, Goicochea E. Lack of developmental toxicity of D-003: a mixture of long-chain fatty acids in rats. *Food Chem Toxicol.* 2003;41(1):89-93.

37. Rodriguez MD, Gonzalez JE, Leon EF, et al. Perinatal/Postnatal Study of D-003, a Mixture of Long-Chain Fatty Acids, in Rats. *J Med Food.* 2006;9(2):223-230.

38. Rodriguez MD, Gonzalez JE, Aleman C, et al. Evaluation of the reproductive and developmental toxicity of the D-003, a mixture of long-chain fatty acids, in rats and rabbits. *Food Chem Toxicol.* 2004;42(12):1977-1985.

39. Aleman CL, Puig MN, Elias EC, et al. Carcinogenicity of policosanol in mice: an 18-month study. *Food Chem Toxicol.* 1995;33(7):573-578.

40. Noa M, Gamez R, Mas R, et al. Study of the long-term carcinogenicity potential of D-003, a mixture of high molecular weight sugarcane wax acids, in mice. *Food Chem Toxicol.* 2009;47(4):687-692.

41. Agata H, Kondo N, Yomo A, et al. Sensitization to sugar cane pollen in Okinawan allergic children. *Asian Pac J Allergy Immunol.* 1994;12(2):151-154.

42. Chakraborty P, Gupta-Bhattacharya S, Chowdhury I, Majumdar MR, Chanda S. Differences in concentrations of allergenic pollens and spores at different heights on an agricultural farm in West Bengal, India. *Ann Agric Environ Med.* 2001;8(2):123-130.

43. Anonymous. 2015. Evaluation of the cutaneous tolerance of a face cosmetic product (rinse-off face mask with 0.36% Saccharum Officinarum (Sugarcane) Extract). (Unpublished data submitted by Personal Care Product Council on January 8, 2021.)

44. Eurofins CRL. 2019. Repeated insult patch test (facial serum containing 1.4% Saccharum Officinarum (Sugarcane) Extract). (Unpublished data submitted by Personal Care Products Council on January 28, 2021.)

45. Consumer Product Testing Co. 2013. Repeated insult patch test (facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract. (Unpublished data submitted by Personal Care Products Council on February 1, 2021.)

FDA – 2021 VCRP DATA – *Saccharum officinarum* (Sugarcane)-Derived Ingredients

Saccharum Officinarum (Sugarcane) Extract

Eye Lotion	1
Hair Conditioner	10
Shampoos (non-coloring)	12
Tonics, Dressings, and Other Hair Grooming Aids	3
Other Hair Preparations	11
Cuticle Softeners	1
Other Manicuring Preparations	1
Bath Soaps and Detergents	27
Other Personal Cleanliness Products	6
Cleansing	20
Depilatories	3
Face and Neck (exc shave)	44
Body and Hand (exc shave)	4
Foot Powders and Sprays	1
Moisturizing	13
Night	1
Paste Masks (mud packs)	12
Skin Fresheners	5
Other Skin Care Preps	36

Total: 211 uses

Saccharum Officinarum (not included in the wINCI Dictionary)

Body and Hand (exc shave)	1
Moisturizing	1
Other Skin Care Preps	2

Total: 4 uses

No VCRP data for Saccharum Officinarum (Sugarcane) Juice Extract, Saccharum Officinarum (Sugarcane) Bagasse Powder, or Saccharum Officinarum (Sugarcane) Wax

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: January 8, 2021

SUBJECT: Saccharum Officinarum (Sugarcane) Extract

Anonymous. 2015. Evaluation of the cutaneous tolerace of a face cosmetic products (rinse-off face mask with 0.36% of Saccharum Officinarum (Sugarcane) Extract).

Study title	**EVALUATION OF THE CUTANEOUS TOLERANCE OF A FACE COSMETIC PRODUCT**
Product	***RINSE-OFF FACE MASK WITH 0.36% OF SACCHARUM OFFICINARUM (SUGARCANE) EXTRACT***
Study dates	From July 6 to 27, 2015
Objective of study	Use test aimed to evaluate the cutaneous tolerance of a cosmetic product under dermatological control.
Application conditions	The product has been applied for 21 days, twice a week, leaved on for 10 minutes and then rinsed-off.
Assessment methods	The clinical quotation is made before and after 21 days of the product use, the subject's face is examined under dermatological control and each of the following parameters is assessed: erythema, edema, dryness, desquamation, roughness, vesicles or other. The subjects are also asked about their sensations: tightness, stinging, itching, warm, burning sensation or other.
Volunteers' characteristics	21 volunteers of the female sex, from 18 to 55 years old, with phototype I to IV, with combination or greasy skin on the face, were analyzed.
Results	After 21 days of twice a week use of the product, one subject reported four functional signs judged not relevant. However, no physical sign was reported and no clinical sign was observed on day 21.
Conclusion	After 21 days of twice a week use, the tested product was very well tolerated on the cutaneous level.

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: January 28, 2021

SUBJECT: Saccharum Officinarum (Sugarcane) Extract

Eurofins CRL. 2019. Repeated insult patch test (facial serum containing 1.44% Saccharum Officinarum (Sugarcane) Extract).

CLINICAL STUDY REPORT

Report Status:	Final
Report Date:	19 July 2019
CRL Study Number:	CRLNJ2019-0436-11
CRL Protocol Number:	CL 1.0 2019
Study Title:	Repeated Insult Patch Test
Test Material:	[redacted]
Sponsor:	[redacted] facial serum contains 1.44% Saccharum Officinarum (Sugarcane) Extract
Sponsor Representative:	[redacted]
Investigating Laboratory:	Eurofins | CRL, Inc. 371 Hoes Lane, Suite 100 Piscataway, New Jersey 08854 Telephone: (732) 981-1616 Fax: (732) 981-0520
Principal Investigator:	Winston Moy, MD Diplomate, American Board of Dermatology
Study Initiation Date:	24 May 2019
Study Completion Date:	05 July 2019

eurofins | CRL

PRINCIPAL INVESTIGATOR SIGNATURE

Study Title: Repeated Insult Patch Test

I have read Clinical Study Report CRLNJ2019-0436-11 and confirm that to the best of my knowledge it accurately describes the conduct and results of the study.

Winston Moy, M.D.

Digitally signed by Winston Moy, M.D.
DN: cn=Winston Moy, M.D., o=Eurofins CRL Inc, ou, email=winston.moy@crlresearchlabs.com, c=US
Date: 2019.07.24 07:36:26 -07'00'

Principal Investigator Signature/Date

Quality Assurance Audit Statement

Clinical Study Number: CRLNJ2019-0436-11

Start Date: 24 May 2019

Completion Date: 05 July 2019

Eurofins | CRL, Inc. 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 Eurofins | CRL, Inc. 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.

Karen Hoyberg

Digitally signed by Karen Hoyberg
DN: cn=Karen Hoyberg, o=Eurofins CRL, Inc., ou=Quality Assurance, email=Karen.Hoyberg@crlresearchlabs.com, c=US
Date: 2019.07.19 11:14:55 -04'00'

Signature of QA Auditor and Date

Table of Contents

CLINICAL STUDY REPORT

Repeated Insult Patch Test (RIPT)

1.0 ETHICS

1.1. ETHICAL CONDUCT OF THE STUDY

Eurofins | CRL, Inc. (CRL) 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 CRL 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 CRL 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 PRINCIPAL INVESTIGATOR AND INVESTIGATIVE SITE

Winston Moy, MD
Diplomate, American Board of Dermatology

Eurofins | CRL, Inc.
371 Hoes Lane, Suite 100
Piscataway, New Jersey 08854
(732)-981-1616

4.0 SPONSOR REPRESENTATIVE AND SPONSOR SITE

[redacted]

5.0 TEST MATERIALS AND RECORD RETENTION

The following test material was provided by [redacted] and was received by Eurofins | CRL, Inc. on 15 April 2019.

Test Material	Test Condition	Patch Type
[redacted]	Neat	Occlusive*

CRL Identification Number
CRLNJ2019-0436-11

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.

5.1. STORAGE AND RETENTION

Prior to study start, the test materials were stored at room temperature and humidity. All unused test materials will be retained by CRL for a minimum of 6 months, in accordance with CRL SOPs.

All original forms of this study will be retained by CRL as specified in CRL Standard Operating Procedures (SOPs).

* Occlusive Strip with Flexcon® (Strukmyer LLC, Mesquite,TX or equivalent)

6.0 RANDOMIZATION

No randomization was required for this study.

7.0 BLINDING

Subjects were not provided with information regarding the identity of the test material. The investigatory staff was not blinded. Test materials were labeled with unique CRL study identification and panel codes and subject numbers upon test material receipt by CRL.

8.0 STUDY DATES

This study was initiated on 24 May 2019 and was completed on 05 July 2019.

9.0 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 (Appendix I).

10.0 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
P = Peeling
S = Spreading of reaction beyond patch site.
Sc = Scabbing
d = Dryness/scaling
D = Oozing, crusting, and/or superficial erosions
I = Itching
F = Follicular irritation with or without pustule formation (folliculitis)
Hr = Hyperpigmentation
Ho = Hypopigmentation
X = Subject Absent
NP = No patching
Pa = Papules
C = Changed site
--- = No reading
B = Burning
SD = Site Discontinued
Ex = Excoriation

11.0 TEST METHOD

This study was conducted according to clinical study protocol CL 1.0 2019.

12.0 STUDY RELATED COMMENTS

Due to the facility being closed for observance of the holiday, all subjects missed their 72 hour challenge visit with the exception of subjects #24 and #82 who started the challenge phase one day late and therefore missed their 48 hour challenge visit.

13.0 STUDY RESULTS

13.1. COMPLETED AND DISCONTINUED SUBJECTS

A total of 105 subjects completed the study. Discontinued subjects are listed below:

Subject Number	Reason for Discontinuation
07	Lost interest
18	Lost to follow up
20	Lost interest
35	Lost to follow up
40	Lost to follow up
67	Lost to follow up
76	Lost to follow up
86	Lost to follow up
87	Lost to follow up
88	Lost to follow up
89	Lost to follow up
92	Lost to follow up
100	Lost to follow up
104	Lost to follow up
109	Lost to follow up

13.2. DERMAL EVALUATIONS

Individual dermal scores recorded during the Induction and Challenge Phases appear in Table I.

13.3. PROTOCOL DEVIATIONS

No protocol deviations occurred over the duration of the study.

13.4. PROTOCOL AMENDMENTS

There were no protocol amendments during this study.

13.5. ADVERSE EVENTS

No adverse events were reported during the study.

14.0 CONCLUSION

Based on the test population of 105 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

Test Material: [redacted]

Subject Number	Induction Scores									Challenge Scores			
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour	96 Hour
1	0	0	0	0	0	0	0	0	0	0	0	X	0
2	0	0	0	0	0	0	0	0	0	0	0	X	0
3	0	0	0	0	0	0	0	0	0	0	0	X	0
4	0	0	0	0	0	0	0	0	0	0	0	X	0
5	0	0	0	0	0	0	0	0	0	0	0	X	0
6	0	0	0	0	0	0	0	0	0	0	0	X	0
7	Discontinued												
8	0	0	0	0	0	0	0	0	0	0	0	X	0
9	0	0	0	0	0	0	0	0	0	0	0	X	0
10	0	0	0	0	0	0	0	0	0	0	0	X	0
11	0	0	0	0	0	0	0	0	0	0	0	X	0
12	0	0	0	0	0	0	0	0	0	0	0	X	0
13	0	0	0	0	0	0	0	0	0	0	0	X	0
14	0	0	0	0	0	0	0	0	0	0	0	X	0
15	0	0	0	0	0	0	0	0	0	0	0	X	0
16	0	0	0	0	0	0	0	0	0	0	0	X	0
17	0	0	0	0	0	0	0	0	0	0	0	X	0
18	0	0	0	0	0	0	Discontinued						
19	0	0	0	0	0	0	0	0	0	0	0	X	0
20	Discontinued												
21	0	0	0	0	0	0	0	0	0	0	0	X	0
22	0	0	0	0	0	0	0	0	0	0	0	X	0
23	0	0	0	0	0	0	0	0	0	0	0	X	0
24	0	0	0	0	0	0	0	0	0	0	X	0	X
25	0	0	0	0	0	0	0	0	0	0	0	X	0
26	0	0	0	0	0	0	0	0	0	0	0	X	0
27	0	0	0	0	0	0	0	0	0	0	0	X	0
28	0	0	0	0	0	0	0	0	0	0	0	X	0
29	0	0	0	0	0	0	0	0	0	0	0	X	0
30	0	0	0	0	0	0	0	0	0	0	0	X	0

Table I - Summary of Dermal Scores (continued)

Test Material: [redacted]

Subject Number	Induction Scores									Challenge Scores			
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour	96 Hour
31	0	0	0	0	0	0	0	0	0	0	0	X	0
32	0	0	0	0	0	0	0	0	0	0	0	X	0
33	0	0	0	0	0	0	0	0	0	0	0	X	0
34	0	0	0	0	0	0	0	0	0	0	0	X	0
35	Discontinued												
36	0	0	0	0	0	0	0	0	0	0	0	X	0
37	0	0	0	0	0	0	0	0	0	0	0	X	0
38	0	0	0	0	0	0	0	0	0	0	0	X	0
39	0	0	0	0	0	0	0	0	0	0	0	X	0
40	Discontinued												
41	0	0	0	0	0	0	0	0	0	0	0	X	0
42	0	0	0	0	0	0	0	0	0	0	0	X	0
43	0	0	0	0	0	0	0	0	0	0	0	X	0
44	0	0	0	0	0	0	0	0	0	0	0	X	0
45	0	0	0	0	0	0	0	0	0	0	0	X	0
46	0	0	0	0	0	0	0	0	0	0	0	X	0
47	0	0	0	0	0	0	0	0	0	0	0	X	0
48	0	0	0	0	0	0	0	0	0	0	0	X	0
49	0	0	0	0	0	0	0	0	0	0	0	X	0
50	0	0	0	0	0	0	0	0	0	0	0	X	0
51	0	0	0	0	0	0	0	0	0	0	0	X	0
52	0	0	0	0	0	0	0	0	0	0	0	X	0
53	0	0	0	0	0	0	0	0	0	0	0	X	0
54	0	0	0	0	0	0	0	0	0	0	0	X	0
55	0	0	0	0	0	0	0	0	0	0	0	X	0
56	0	0	0	0	0	0	0	0	0	0	0	X	0
57	0	0	0	0	0	0	0	0	0	0	0	X	0
58	0	0	0	0	0	0	0	0	0	0	0	X	0
59	0	0	0	0	0	0	0	0	0	0	0	X	0
60	0	0	0	0	0	0	0	0	0	0	0	X	0

Table I - Summary of Dermal Scores (continued)

Test Material: [redacted]

Subject Number	Induction Scores									Challenge Scores			
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour	96 Hour
61	0	0	0	0	0	0	0	0	0	0	0	X	0
62	0	0	0	0	0	0	0	0	0	0	0	X	0
63	0	0	0	0	0	0	0	0	0	0	0	X	0
64	0	0	0	0	0	0	0	0	0	0	0	X	0
65	0	0	0	0	0	0	0	0	0	0	0	X	0
66	0	0	0	0	0	0	0	0	0	0	0	X	0
67	Discontinued												
68	0	0	0	0	0	0	0	0	0	0	0	X	0
69	0	0	0	0	0	0	0	0	0	0	0	X	0
70	0	0	0	0	0	0	0	0	0	0	0	X	0
71	0	0	0	0	0	0	0	0	0	0	0	X	0
72	0	0	0	0	0	0	0	0	0	0	0	X	0
73	0	0	0	0	0	0	0	0	0	0	0	X	0
74	0	0	0	0	0	0	0	0	0	0	0	X	0
75	0	0	0	0	0	0	0	0	0	0	0	X	0
76	0	0	0	0	0	Discontinued							
77	0	0	0	0	0	0	0	0	0	0	0	X	0
78	0	0	0	0	0	0	0	0	0	0	0	X	0
79	0	0	0	0	0	0	0	0	0	0	0	X	0
80	0	0	0	0	0	0	0	0	0	0	0	X	0
81	0	0	0	0	0	0	0	0	0	0	0	X	0
82	0	0	0	0	0	0	0	0	0	0	X	0	X
83	0	0	0	0	0	0	0	0	0	0	0	X	0
84	0	0	0	0	0	0	0	0	0	0	0	X	0
85	0	0	0	0	0	0	0	0	0	0	0	X	0
86	0	0	0	0	Discontinued								
87	0	0	0	0	Discontinued								
88	0	0	0	Discontinued									
89	Discontinued												
90	0	0	0	0	0	0	0	0	0	0	0	X	0

Table I - Summary of Dermal Scores (continued)

Test Material: [redacted]

Subject Number	Induction Scores									Challenge Scores			
	1	2	3	4	5	6	7	8	9	24 Hour	48 Hour	72 Hour	96 Hour
91	0	0	0	0	0	0	0	0	0	0	0	X	0
92	Discontinued												
93	0	0	0	0	0	0	0	0	0	0	0	X	0
94	0	0	0	0	0	0	0	0	0	0	0	X	0
95	0	0	0	0	0	0	0	0	0	0	0	X	0
96	0	0	0	0	0	0	0	0	0	0	0	X	0
97	0	0	0	0	0	0	0	0	0	0	0	X	0
98	0	0	0	0	0	0	0	0	0	0	0	X	0
99	0	0	0	0	0	0	0	0	0	0	0	X	0
100	Discontinued												
101	0	0	0	0	0	0	0	0	0	0	0	X	0
102	0	0	0	0	0	0	0	0	0	0	0	X	0
103	0	0	0	0	0	0	0	0	0	0	0	X	0
104	0	0	0	Discontinued									
105	0	0	0	0	0	0	0	0	0	0	0	X	0
106	0	0	0	0	0	0	0	0	0	0	0	X	0
107	0	0	0	0	0	0	0	0	0	0	0	X	0
108	0	0	0	0	0	0	0	0	0	0	0	X	0
109	0	0	0	Discontinued									
110	0	0	0	0	0	0	0	0	0	0	0	X	0
111	0	0	0	0	0	0	0	0	0	0	0	X	0
112	0	0	0	0	0	0	0	0	0	0	0	X	0
113	0	0	0	0	0	0	0	0	0	0	0	X	0
114	0	0	0	0	0	0	0	0	0	0	0	X	0
115	0	0	0	0	0	0	0	0	0	0	0	X	0
116	0	0	0	0	0	0	0	0	0	0	0	X	0
117	0	0	0	0	0	0	0	0	0	0	0	X	0
118	0	0	0	0	0	0	0	0	0	0	0	X	0
119	0	0	0	0	0	0	0	0	0	0	0	X	0
120	0	0	0	0	0	0	0	0	0	0	0	X	0

Appendix I - Subject Demographics

Subject Number	Age	Sex
1	55	F
2	27	F
3	53	F
4	53	F
5	58	F
6	68	F
7	43	F
8	43	F
9	61	F
10	28	M
11	45	F
12	50	F
13	67	M
14	47	F
15	59	M
16	54	F
17	70	F
18	18	F
19	42	F
20	53	F
21	68	M
22	60	F
23	64	F
24	42	F
25	62	F
26	57	F
27	48	F
28	66	F
29	19	M
30	61	F

Subject Number	Age	Sex
31	29	F
32	47	F
33	49	F
34	55	M
35	39	F
36	24	M
37	66	M
38	61	F
39	60	F
40	43	F
41	47	F
42	57	F
43	69	F
44	64	F
45	22	F
46	32	M
47	67	F
48	30	F
49	51	F
50	36	M
51	67	F
52	69	M
53	66	F
54	55	F
55	30	M
56	57	F
57	61	M
58	61	F
59	21	F
60	57	M

Appendix I – Subject Demographics (continued)

Subject Number	Age	Sex
61	29	F
62	63	F
63	47	F
64	59	F
65	57	F
66	51	F
67	19	F
68	44	F
69	32	F
70	55	F
71	57	F
72	54	F
73	28	F
74	62	F
75	48	F
76	56	F
77	55	F
78	24	M
79	56	F
80	62	F
81	45	F
82	22	F
83	68	F
84	61	F
85	33	F
86	50	F
87	47	F
88	21	M
89	56	M
90	48	M

Subject Number	Age	Sex
91	58	F
92	29	M
93	53	M
94	50	F
95	20	M
96	40	F
97	45	F
98	70	M
99	52	M
100	26	F
101	58	F
102	64	F
103	31	F
104	54	F
105	41	F
106	25	F
107	37	F
108	41	M
109	26	F
110	59	F
111	52	M
112	66	F
113	56	F
114	61	F
115	69	F
116	31	F
117	49	F
118	55	F
119	57	F
120	65	F

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 1, 2021

SUBJECT: Saccharum Officinarum (Sugarcane) Extract

Consumer Product Testing Co. 2013. Repeated insult patch test (facial moisturizer containing 2.7% Saccharum Officinarum (Sugarcane) Extract).

Consumer Product Testing Co.

EST. 1975

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test
Protocol No.: CP-01.01S

TEST MATERIAL: NIGHT MOISTURIZER- ENG064180, 7878-9

contains 2.7% Saccharum Officinarum (Sugarcane) Extract

EXPERIMENT REFERENCE NUMBER: C13-1798.01

Reviewed by: Richard R. Eisenberg, M.D.
Medical Director
Board Certified Dermatologist

Approved by: Michael Caswell, Ph.D., CCRA, CCRC
Vice President, Clinical Evaluations
05 Jun 2013

Approved by: Joy Frank, R.N.
Executive Vice President, Clinical Evaluations
6/6/13

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234

Consumer Product Testing Co.
EST. 1973

QUALITY ASSURANCE UNIT STATEMENT

Study Number: C13-1798.01

The Consumer Product Testing Company, Incorporated (CPTC) Quality Assurance Unit (QAU) is responsible for auditing the conduct, content and reporting of all clinical trials that are conducted at CPTC.

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

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

All records and documents pertaining to the conduct of this trial shall be retained in the CPTC archives for a minimum of ten (10) years. At any time prior to the completion of the tenth archival year, a Sponsor may submit a written request to the CPTC QAU to obtain custody of trial records once the CPTC archive period has been completed. This transfer shall be performed at the Sponsor's expense. In the absence of a written request, trial-related records shall be destroyed at the end of the CPTC archive period in a manner that renders them useless.

Quality Assurance Representative

6/7/13
Date

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

Participants: One hundred thirteen (113) qualified subjects, male and female, ranging in age from 19 to 70 years, were selected for this evaluation. One hundred five (105) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

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

Exclusion Criteria:

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

Test Material: NIGHT MOISTURIZER- ENG064180, 7878-9

Study Schedule:

Panel #	Initiation Date	Completion Date
20130141	April 15, 2013	May 23, 2013
20130145	April 22, 2013	May 31, 2013

[a]With parental or guardian consent

Methodology:

The upper back between the scapulae served as the treatment area. Approximately 0.2 g of the test material, or an amount sufficient to cover the contact surface, was applied to the 1" x 1" absorbent pad portion of a clear adhesive dressing. This was then applied to the appropriate treatment site to form a semi-occlusive patch.

Induction Phase:

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

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

Rest periods consisted of twenty-four hours following each Tuesday and Thursday removal, and forty-eight hours following each Saturday removal.

Challenge Phase:

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

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

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

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

Adverse Events: There were no adverse events.

Amendments: There were no amendments.

Deviations: There were no deviations.

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

Observations remained within normal limits throughout the test interval.

Subject demographics are presented in Table 2.

Summary: Under the conditions of this study, test material, NIGHT MOISTURIZER-ENG064180, 7878-9, did not indicate a potential for dermal irritation or allergic contact sensitization.

[redacted]
C13-1798.01

Table 1
Panel #20130141

Individual Results

NIGHT MOISTURIZER- ENG064180, 7878-9

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------					
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	----------DID NOT COMPLETE STUDY----------									
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch

Table 1
(continued)
Panel #20130141

Individual Results

NIGHT MOISTURIZER- ENG064180, 7878-9

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	----------DID NOT COMPLETE STUDY----------						
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	**0.5**	**0.5**	0	**0.5**	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0[m]	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
m = Additional makeup day granted at the discretion of the clinic supervisor

[redacted]
C13-1798.01

Table 1
(continued)
Panel #20130145

Individual Results

NIGHT MOISTURIZER- ENG064180, 7878-9

Subject Number	24*hr	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site 24*hr	72 hr
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	---DID NOT COMPLETE STUDY---					
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	-	0	0	0	0	0	0	0	0	0	0	0
12	-	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0	0	0	0
20	---DID NOT COMPLETE STUDY---											
21	-	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0	0
26	-	0	0	---DID NOT COMPLETE STUDY---								
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
- = Subject not present for supervised removal

Table 1
(continued)
Panel #20130145

Individual Results

NIGHT MOISTURIZER- ENG064180, 7878-9

Subject Number	Induction Phase									Virgin Challenge Site	
	24*hr	1	2	3	4	5	6	7	8	9	24*hr	72 hr
30	DID NOT COMPLETE STUDY											
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	DID NOT COMPLETE STUDY			
48	-	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0

24* = Supervised removal of 1st Induction and Challenge Patch
- = Subject not present for supervised removal

Table 2
Panel #20130141

Subject Demographics

Subject Number	Initials	Age	Sex
1	JFH	44	M
2	AMC	35	F
3	AJC	30	F
4	CJC	52	M
5	JLV	41	F
6	DMD	53	F
7	DPB	65	M
8	H-B	54	M
9	SEV	68	F
10	JAT	48	M
11	ADC	39	M
12	M-Z	51	F
13	L-W	47	M
14	MRH	22	F
15	M-D	54	F
16	A-M	47	M
17	RAD	41	M
18	D-M	46	F
19	C-S	45	F
20	LAK	48	F
21	PVO	41	F
22	NHB	45	F
23	LMO	46	F
24	NLJ	57	F
25	RVD	55	M
26	E-M	54	F
27	ELM	32	F
28	PGH	48	F
29	QLD	33	F

Table 2
(continued)
Panel #20130141

Subject Demographics

Subject Number	Initials	Age	Sex
30	JGM	50	F
31	R-M	28	M
32	DPC	57	F
33	D-R	61	F
34	MAE	46	M
35	MSL	60	F
36	DWM	52	M
37	CPW	57	M
38	B-C	49	F
39	SCF	43	F
40	RDF	44	M
41	EAS	58	F
42	MEP	70	F
43	J-B	52	M
44	MPF	52	M
45	L-C	57	M
46	JMN	54	F
47	JMC	25	F
48	MLA	55	F
49	DMJ	47	F
50	JFK	69	F
51	L-H	25	F
52	BWC	52	M
53	SAM	19	M
54	BJS	43	F
55	D-N	27	F
56	DSP	41	F

Table 2
(continued)
Panel #20130145

Subject Demographics

Subject Number	Initials	Age	Sex
1	AMS	66	M
2	H-H	52	M
3	JJR	23	F
4	DMR	62	F
5	SLR	31	F
6	T-H	35	F
7	ISM	22	F
8	E-W	47	F
9	MTR	52	F
10	M-G	67	F
11	CSG	26	F
12	MAM	36	F
13	RLA	44	M
14	LMP	61	F
15	L-R	45	F
16	YYM	31	F
17	SAR	37	F
18	LAM	47	F
19	DMB	42	F
20	SMR	33	F
21	SAM	43	M
22	L-F	65	F
23	R-F	67	M
24	SKC	28	F
25	AMR	23	F
26	BMJ	28	M
27	MYS	34	M
28	E-B	65	F
29	NMD	27	F

Table 2
(continued)
Panel #20130145

Subject Demographics

Subject Number	Initials	Age	Sex
30	UPP	62	F
31	DAW	48	F
32	EJG	22	M
33	L-S	39	F
34	BWP	53	M
35	BLA	59	F
36	RLS	56	F
37	SMH	51	F
38	M-C	48	F
39	S-R	53	F
40	DSP	21	F
41	C-S	28	F
42	TOK	28	M
43	E-B	43	F
44	S-K	57	F
45	SLK	34	F
46	DVJ	40	F
47	JEJ	29	M
48	LDS	27	F
49	A-A	61	F
50	DRB	69	M
51	LCO	54	F
52	E-F	38	F
53	A-S	45	M
54	M-D	43	M
55	A-G	48	M
56	EAS	20	M
57	GJG	49	M