Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Status:	Draft Tentative Report for Panel Review
Release Date:	August 20, 2021
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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; 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 Christina L. Burnett, Senior Scientific Analyst/ Writer, CIR.

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Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: August 20, 2021
Subject: Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Tentative Report of the Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics. (It is identified as *barley092021rep* in the pdf document.) At the December 2020 meeting, the Panel issued an Insufficient Data Announcement (IDA). The additional data needed to determine safety for these 16 cosmetic ingredients are:

- 28-day dermal toxicity data on the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    - If positive, developmental and reproductive toxicity and genotoxicity data may be needed
    - Alternatively, acceptable evidence of safe use as a food for ingredients derived from the flower, leaf, stem and root
- Dermal irritation and sensitization data at maximum concentration of use for the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract

Since the issuance of the IDA, CIR has received unpublished human dermal irritation data, an ocular in-use study, and an HRIPT on a mascara containing 0.3% Hordeum Distichon (Barley) Extract (b*arley092021data1*), and HRIPTs on cosmetic products containing up to 2.76% Hordeum Distichon (Barley) Extract and 0.005% Hordeum Vulgare Extract (*barley092021data2*). These data have been incorporated into the report and are highlighted to aid in the Panel's review.

The Use Table has been updated with the 2021 VCRP data (*barley092021fda*). Uses for Hordeum Vulgare Extract decreased from 383 to 167. The majority of the uses are in leave-on makeup preparations and skin care products. Uses also decreased for Hordeum Distichon (Barley) Extract, from 91 to 30. The majority of the uses for this ingredient in is leave-on skin care products. Additionally, use has now been reported for Hordeum Vulgare Seed Flour (2 total uses; one was generically described as "barley flour" in the VCRP).

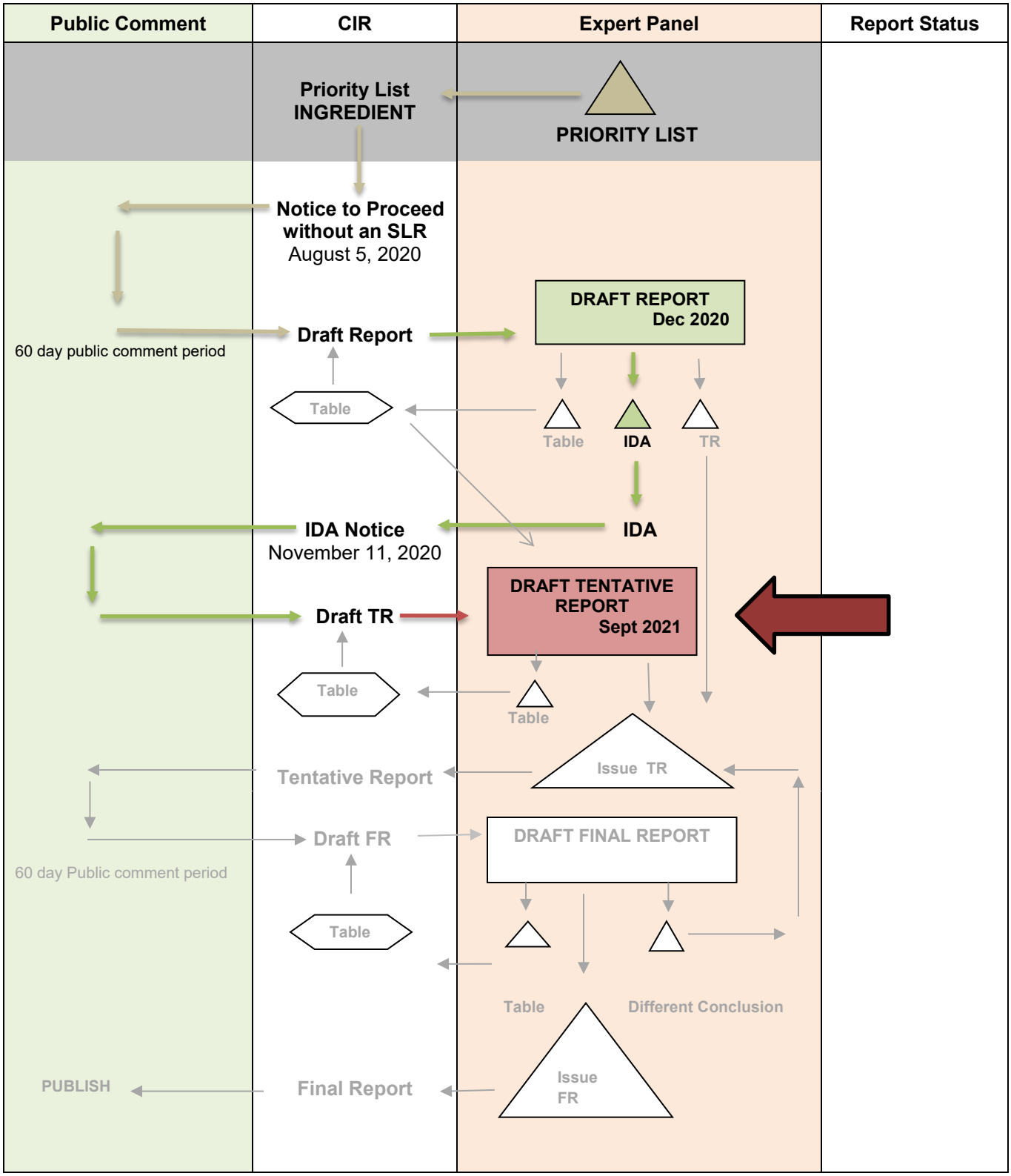
Additional supporting documents for this report package include a flow chart (*barley092021flow*), report history (*barley092021hist*), minutes (*barley092021min*), a search strategy (*barley092021strat*), and a data profile (*barley092021prof*).

The Panel should carefully consider and discuss the data (or lack thereof), and issue a Tentative Report with a safe, safe with qualifications, insufficient data, unsafe, or split conclusion.

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Barley-derived Ingredients

MEETING September 2021



Barley-Derived Ingredients History

August 5, 2020 – Notice to Proceed issued.

August – October 2020 – Unpublished data received.

December 2020 – The Panel issued an IDA. The additional data needed to determine safety for these cosmetic ingredients are:

- 28-day dermal toxicity data on the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
    - If positive, developmental and reproductive toxicity and genotoxicity data may be needed
    - Alternatively, acceptable evidence of safe use as a food for ingredients derived from the flower, leaf, stem and root
- Dermal irritation and sensitization data at maximum concentration of use for the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract

January-February 2021 – Additional unpublished data received.

Barley-Derived Ingredients Data Profile* – September 2021 – Christina Burnett

					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/Human	Retrospective/ Multicenter	Case Reports	In-Use
Hordeum Distichon (Barley) Extract	X		X	X																	X			X						X
Hordeum Distichon (Barley) Seed Flour			X	X																										
Hordeum Vulgare Extract	X																				X			X						X
Hordeum Vulgare Flower/Leaf/Stem Juice																														
Hordeum Vulgare Juice				X																										
Hordeum Vulgare Leaf Extract	X																													
Hordeum Vulgare Leaf Juice																														
Hordeum Vulgare Leaf Powder																														
Hordeum Vulgare Leaf/Stem Powder																														
Hordeum Vulgare Powder																														
Hordeum Vulgare Root Extract																														
Hordeum Vulgare Seed Extract	X		X	X																				X						
Hordeum Vulgare Seed Flour			X	X																										
Hordeum Vulgare Seed Water			X																											
Hordeum Vulgare Sprout Extract				X																										
Hordeum Vulgare Stem Water																														
Barley flour - generic	X																													
Barley - generic		X		X																									X	

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

Barley-Derived Ingredients

Ingredient	CAS #	PubMed	FDA	EU	ECHA	SCCS	SIDS	ECETOC	HPVIS	AICIS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Hordeum Vulgare Extract	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Flower/Leaf/Stem Juice	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Juice	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Leaf Extract	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Leaf Juice	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Leaf Powder	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Leaf/Stem Powder	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Powder	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Root Extract	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Seed Extract	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Seed Flour	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Seed Water	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Sprout Extract	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Vulgare Stem Water	85251-64-5	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Distichon (Barley) Extract	85251-64-5; 94349-67-4	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Hordeum Distichon (Barley) Seed Flour	None	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Botanical and/or Fragrance Websites (if applicable)

Ingredient	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	AHPA	EMA	AGRICOLA	IFRA	RIFM
Hordeum vulgare (generic)	√	√	√	√	√	√	√	√	√
Hordeum distichon (generic)	√	√	√	√	√	√	√	√	√

Search Strategy

PubMed

Hordeum Vulgare Extract: 1009 results, 23 relevant
Hordeum Vulgare Flower/Leaf/Stem Juice: 0 results
Hordeum Vulgare Juice: 18 results, 4 relevant
Hordeum Vulgare Leaf Extract: 167 results, 10 relevant
Hordeum Vulgare Leaf Juice: 4 results, 2 relevant
Hordeum Vulgare Leaf Powder: 7 results, 2 relevant
Hordeum Vulgare Leaf/Stem Powder: 0 results
Hordeum Vulgare Powder:45 results, 3 relevant
Hordeum Vulgare Root Extract: 103 results, 3 relevant
Hordeum Vulgare Seed Extract: 307 results, 16 relevant
Hordeum Vulgare Seed Flour: 76 results, 16 relevant
Hordeum Vulgare Seed Water: 267 results, 0 relevant
Hordeum Vulgare Sprout Extract: 12 results, 3 relevant
Hordeum Vulgare Stem Water: 33 results, 1 relevant
Hordeum Distichon (Barley) Extract: 3 results, 1 relevant
Hordeum Distichon (Barley) Seed Flour: 0 results

Searches were narrowed down in some cases to exclude “malt” and “germination” and “genotype”.

Barley Dermal Toxicity: 2 hits, 0 relevant
Barley Systemic Toxicity: 18 hits, 2 relevant
Barley Genotoxicity: 56 hits, 0 relevant
Barley Extract Chemical Composition NOT Fermented: 833 hits, 16 relevant

Search updated July 2021. No new relevant references.

According to the NCBI Taxonomy Database and the U.S. National Plant Germplasm System, Hordeum distichon is a subspecies of Hordeum vulgare.

LINKS

Search Engines

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

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

Pertinent Websites

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

- International Programme on Chemical Safety http://www.inchem.org/
- FAO (Food and Agriculture Organization of the United Nations) - http://www.fao.org/food/food-safety-quality/scientific-advice/jecfa/jecfa-additives/en/
- WHO (World Health Organization) technical reports - http://www.who.int/biologicals/technical_report_series/en/
- www.google.com - a general Google search should be performed for additional background information, to identify references that are available, and for other general information

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
- 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) – https://ifrafragrance.org/
- Research Institute for Fragrance Materials (RIFM) - https://www.rifm.org/#gsc.tab=0

DECEMBER 2020 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito's Team Meeting – December 7, 2020

DR. BELSITO: Okay. So now we're moving on to barley. And again, this is the only one that we got some additional data with an HRIPT. So Christina, the first question I have is under toxicologic studies, you say most of the barley ingredients are found in foods. Is that true for the stem, leaf, and root? I thought it was just seed and malt that were food.

MS. BURNETT: Let me get down to the part where you're -- yeah. I don't know what the leaf and the stems --

DR. BELSITO: And the root.

MS. BURNETT: And the root, correct. But I could alter that to say most of -- the seed.

DR. BELSITO: Seed and the malt in food.

MS. BURNETT: Right. I did not -- unlike wheat, where people make juice out of wheatgrass, I did not necessarily see anything similar for barley grass.

DR. BELSITO: So the data that we got on sensitization in Wave 2 bothered me a little bit because there was apparent irritation. But there was also, I thought, the possibility of sensitization in subjects eight and ten, because they were negative during the entire induction period, and they did have some minimal responses that persisted out.

Now, it was a 1.8 percent lotion. It's entirely possible that it was 98.2 percent one of those other ingredients that caused this. But I don't think we really have sufficient sensitization data on this, was just my feeling. And so, I thought that we needed sensitization and irritation, still, and concentration of use. And the question is, do we need a 28-day dermal on the materials that aren't used as foods?

DR. SNYDER: So I agreed with you on the sensitization. The *vulgare* extract is -- the maximum use concentration is 1.5 percent. We don't have any sensitization at that level. And then also the *vulgare* extract has the most uses, and we don't have any method of manufacture or composition. So I agree that we probably need a 28-day dermal on that. Because we only have it on the seed flour, the seed extract, and the seed water. So I was kind of in that same ballpark.

DR. LIEBLER: So I'd modify that slightly, Paul, to say that a method of manufacture I think we're okay on. Because the *distichon* extract is a whole plant extract, and it's briefly but adequately described. And I think that we can infer that that also would apply to the *vulgare*.

DR. SNYDER: Okay. As long as that's -- as long as you -- I just didn't know if we could or not, so.

DR. LIEBLER: Because they're both whole plant extracts and they -- now, as far as composition, we've got very minimal description of the composition of *distichon*, barley extract, just to say that it didn't have any heavy metals or pesticides. But it doesn't say much else, except the 26 fragrance allergens defined by European Union cosmetic regulations were below threshold. But beyond that, the whole plant extracts aren't described with respect to composition and impurities, or at least composition.

So I agree with you, we're short on composition. We don't have anything in here that we could reasonably use to infer for the whole plant. Everything else, in terms of composition, are the seed-related stuff except for the juice.

DR. BELSITO: Yeah. I put composition data on barley extract, seed, flour, juice, seed extracts, sprout extract, were really very generic, and I question whether they were adequate.

DR. LIEBLER: Yeah. The juice is very similar to the whole plant extract, except you just basically make the Juice, you just squeeze the hell out of it and collect what comes out. So it's probably quite related, but the description for juice is very minimal.

DR. BELSITO: So we have manufacturing for barley extract, seed flour, seed extract and seed water. But we still need composition for those or --

DR. LIEBLER: Well, the composition for those -- for the seed stuff -- is actually quite good overall. So I'm not worried about composition there or method of manufacture for anything seed related. It's the whole plant extract is the main issue, because those are the most heavily used ingredients apparently.

DR. SNYDER: The only ones used.

DR. LIEBLER: Yeah.

DR. BELSITO: The manufacture, composition, and impurities for the whole plant extract?

DR. LIEBLER: Right. I would say composition and impurities. Method of manufacture -- well, I'll tell you what, let's ask for it now. Fall back is that we might be able to go with what we have for the *distichon* barley extract, method of manufacture. That's the first item under method of manufacture, PDF 11. Because I think that would apply to *vulgare* as well.

DR. BELSITO: Okay. So we need --

DR. LIEBLER: Composition and impurities are all we need really.

DR. BELSITO: I missed what you said, Dan. You broke up.

DR. LIEBLER: Oh. I said that all we need, really, is the composition and impurities on the *distichon* and *vulgare* extracts.

DR. BELSITO: For both of them, or will one suffice for the other?

DR. LIEBLER: Let's ask for both, and we can fall back to using one.

DR. BELSITO: Okay. And are we asking for concentration of use for the ones we don't? Right now we have concentration of use for the *vulgare* and the *distichon*. And we've got reported uses for leaf extract, seed extract, got barley flour but no concentration of use. Or would we assume that the maximum concentration would be 1.5 or whatever the max is here? I forget.

MS. BURNETT: One point eight.

DR. BELSITO: One point eight, thank you.

DR. SNYDER: Rather a standard thing that those aren't reported or that those --

DR. BELSITO: No. They are reported to be used, at least VCRP leaf extract, seed extract, barley flour, but we don't have a concentration of use.

MS. BURNETT: Well, they have been surveyed by the council.

DR. BELSITO: I realize that. What I'm saying is, do we ask for it again? Or do we assume that the maximum concentration for those would be 1.8?

MS. FIUME: Typically in our conclusions, we use the footnote that says that that would be assumption for the maximum concentration of use.

DR. BELSITO: Okay. So we don't need that then. We need sensitization and irritation data at concentration of use. I mean, it would be ideal if they did it. And I think this was mentioned, in the council notes that I looked at this morning, that that last wave, that that could be due to the fact that it was a whole lotion that was tested. Just as with

the one we previously looked at, it turned that they were doing a HRIPT on a rinse-off product, which is not reasonable. But I think we still need sensitization and irritation. What about a 28-day dermal for the components that aren't GRAS, or are we fine with those? So that would be the --

DR. LIEBLER: Well, that's the two most heavily used ingredients, really. It's the two extracts, the *vulgare* and *distichon*.

DR. BELSITO: Right. So do we want a 28-day dermal on those? Because the whole extract includes the stem, the leaf, and the root, right?

DR. LIEBLER: Right. Well, it may not include the root. It depends on whether they harvest these things by mowing them or pulling them up. I would bet the former.

DR. BELSITO: Right.

DR. LIEBLER: So I think that we should ask for 28-day dermal, because we don't have anything to fall back on in terms of safety.

DR. BELSITO: Okay. So we want a 28-day dermal on the --

DR. EISENMANN: But young shoots of barley, barley grass is eaten as a food, just --

DR. SNYDER: Yeah. I think we need clarification on what is GRAS, because I think it's more than just the kernel.

DR. EISENMANN: Yeah. I think just the kernel is eaten. I think you can eat young barley.

DR. SNYDER: Yeah. Right.

DR. LIEBLER: So if that were clarified, Carol, that would really -- that would remove my concern. I wouldn't be looking to get a 28-day dermal then.

DR. BELSITO: Okay. So we want to clarify what's GRAS. And if the stem and the leaf aren't GRAS, then we'd want a 28-day dermal on the whole plant extract? Is that it?

DR. LIEBLER: Yeah.

MS. BURNETT: What about the root?

DR. LIEBLER: Oh the root same. And the root we really got nothing. I can't even infer method of manufacture and composition and impurities for the root.

DR. BELSITO: So if we don't know that the whole plant extract doesn't include the root, does that help us at all, because the roots not going to be grass?

DR. LIEBLER: Yeah. No. I think that it -- I think that it doesn't help us. I just still think we need the whole plant extract. It either needs to be clear evidence that it's widely consumed as a food, or we'll need 28-day dermal, because we'll have no tox on it.

DR. BELSITO: Right. Okay. So what I have is we want manufacture, composition, impurities for the whole *distichon* and *vulgare* extract. Sensitization and irritation on those at concentration of use. And a 28-day dermal on the whole plant extract to clear tox endpoints or clarify what's grass.

DR. SNYDER: You got it.

DR. LIEBLER: Yep.

DR. BELSITO: Okay. And then we can start the discussion with the botanical and respiratory boilerplates.

MS. FIUME: And I'm sorry. Were there specific requests for the root as well? Or did they fall under what was already listed by Don?

DR. LIEBLER: We need a --

DR. BELSITO: Well, I -- go ahead, Dan.

DR. LIEBLER: Method of manufacture, composition impurities, 28-day dermal, unless people eat it.

MS. FIUME: Thank you.

DR. BELSITO: Anything else? Okay.

MS. FIUME: Can I just ask for a point of clarification from Carol, actually. Because talking about the rinse-off products in sensitization testing this is, I believe, the second time it came up. Carol, is that just a clarification of the type of product that's being tested, or are they actually doing a rinse off during the testing? I don't know if Carol's still here.

DR. EISENMANN: Yeah. I'm here. It just took me a while to get to the Unmute button, sorry. Generally, it's the type of product that was tested. And generally, when they do rinse-off products, they dilute them a lot before they test them in an HRIPT.

MS. FIUME: And when you submit to us, we do know what the actual test concentration is?

DR. EISENMANN: Usually, yes.

MS. FIUME: All right, thank you.

DR. BELSITO: Now Dan, in addition to asking for composition impurities for the whole plant extract, are you specifically asking also for the root on the assumption that the plant extract doesn't include the root?

DR. LIEBLER: That is correct.

DR. BELSITO: Okay.

DR. LIEBLER: If they can show that -- if they can show that the plant extract includes the root, the plant extract would clear the root of course.

DR. BELSITO: Okay. So manufacture, composition, and impurities on the whole plant extract and the root, sensitization and irritation at concentration of use of the whole plant extract, and a 28-day dermal on the whole plant extract to clear the tox endpoints and clarify what's grass.

DR. LIEBLER: Yep.

DR. BELSITO: Okay. Anything else? Okay.

Cohen's Team Minutes – December 7, 2020

DR. COHEN: Just one also procedural comment. When you're using the internet link for the data, there's no page numbers. So, when you refer to a PDF page, it ought to appear on using the online versions.

DR. HELDRETH: Okay.

DR. COHEN: So you have to download all of them and then they get page numbers assigned. I don't know if in the future, if we're using this method of data distribution, whether there should be some page numbers online.

DR. HELDRETH: Yeah, I mean, that's something we could do. I mean, we've at least in the time I've been with the Panel, we've kind of went back and forth on do we use the PDF page numbers, or do we add page numbers, and what confusion there is. But, if the Panel consensus is to change the format and add those page numbers, we'd be happy to do that.

DR. COHEN: I would say it just depends on if you're -- they used to come on drives, right?

DR. HELDRETH: Yes.

DR. COHEN: Now they're coming through on these hotlinks on the agenda, so there's a new distribution method.

DR. HELDRETH: True.

DR. COHEN: That's just something for consideration. If we use the PDF numbers, we'll just download them, and then we'll have PDF numbers.

DR. HELDRETH: Okay. Yeah, we can definitely consider that.

DR. COHEN: Okay. So we have the barley-derived ingredients. This is Christina's as well. This is a draft report. It's the first time we're reviewing this. This safety assessment has 16 derived ingredients. It's used as a skin conditioning agent, abrasive antioxidant, and bulking agent.

We have max concentration of use for the Vulgare extract at 1.5 in leave-on products, and this distichon extract at 1.8 percent in leave-on products. And no concentrations were reported on two in-use, barley-derived ingredients, and that 12 ingredients not reported to be in use in the VCRP, manufacturing for the distichon extract, seed flour, Vulgare seed flour, and Vulgare seed extract, and seed water. So can we read across with this table of 16 products?

DR. SLAGA: One thing just to remind, this is consumed by humans and animals, so there's a lot of data on its safety. I had that they all were safe except for the leaf ingredients, which we have very little data or no data. And for that, we would need genotoxicity and skin irritation data. The sensitization is in Wave 2, and that seems to be okay.

DR. COHEN: Ron?

DR. SHANK: Okay. I'm not too sure of the flower/ leaf/stem juice is a food or the leaf -- anything from the leaf is a food whether the extract is a food.

DR. SLAGA: That's the whole plant, it says.

DR. SHANK: If we can be sure those are not foods, then we need 28-day dermal, genotox, DART, irritation, and sensitization data.

DR. COHEN: Which one, Ron?

DR. SHANK: On the Vulgare. On the Hordeum Vulgare series where the leaf -- there are several leaf products and then the root extract and a stem water. I don't see how those are foods, but maybe they are. That would be

Hordeum Vulgare flower/leaf/stem juice, leaf extract, leaf juice, leaf powder, leaf/stem powder, root extract, and stem water. So there are seven of them.

And if they're not foods, then we need 28-day dermal, genotox, developmental and reproductive tox, dermal irritation and sensitization. The HRIPT info that we have on the Vulgare is at too low a concentration -- 0.005 percent -- when the max concentration is 1.5 percent. So, although we have HRIPT data for the Vulgare extract, it's not high enough.
We do have sensitization data on the distichon -- I guess it's pronounced -- distichon extract at the maximum concentration, 1.8 percent. It was not a sensitizer, so that part is okay. If the seven ingredients I mentioned are eaten by humans, then we don't need the systemic tox data.

DR. SLAGA: I had also root and all leaf ingredients, which are the main ones that you talked about.

DR. SHANK: Yes.

DR. SLAGA: The whole plant is eaten by animals. I don't know about humans.

DR. BERGFELD: Well, secondarily by humans.

DR. PETERSON: I don't think that counts.

DR. SLAGA: It doesn't count? A cat will eat it. And they don't get any --

DR. PETERSON: I have a -- I mean, ca- -- we have another ingredient if cats and dogs eat it they get sick, and humans don't, so I think we have to be careful.

Anyway, I'm -- I have a question because I'm not clear for the extracts, the barley extracts. Was that an X for the -- and they're the most used. Is that just the seed, the part that we eat? I was under the impression it was the whole plant -- the whole barley plant, was extracted for the barley extracts, for the two that are the highest use.

MS. BURNETT: According to the definition in the *Cosmetic Ingredient Dictionary*, it's the whole plant.

DR. PETERSON: Okay. So, therefore, I was wondering -- I felt that we could use the method of manufacturing and the constituent and impurities for the two -- I guess I'm still struggling if it's species/genus of barley plant -- that they might be equivalent.

There is a nice discussion about how growing -- you have different cultivars. You have hugely different constituents, and so I was wondering -- what I was trying to figure out, from some of the references, where they were comparing different cultivars, if some of those cultivars were also the distichon genus/species. And, if there was such a wide range that, perhaps, the Hordeum Distichon extract and the Vulgare extract could be read across for those two things.

And then I was wondering -- so it's like the one that's highest use, you have the dermal information, but you don't have method of manufacturing, constituents, or impurity. No, you have constit- -- Yeah, actually, there is information about the constituents for the Vul- -- it seemed where most of the information was available. And that because they were whole plants, that there might be some read across to the other items.

I mean, this is a question I had. I know they're extracts, and if that's going to impact what gets extracted. But I think this is the complexity of the botanicals, because it was clear from, actually, all the data you provided, Christina, that there was huge variations between different cultivars. And where they were grown, there was also a big difference.

So, I mean, you can't actually expect that the cosmetic community is going to need to provide safety information depending on the country they got their barley from. So I was wondering how much read across could be done. Given the wide variety of stuff, perhaps, one could be more liberal than one might normally be. Because you have the same constituents that the amounts of which vary enormously depending on where they're grown and what cultivar is used.

MS. BURNETT: And it could also depend on just the environmental conditions any given year.

DR. COHEN: Yeah.

MS. BURNETT: Based on what I read, barley's very hardy, and it is preferred to be grown in the Middle East because it is very drought resistant. With all these botanicals, it always depend- -- that is something that always considers, you know, every year's different, where they are grown is different.

DR. PETERSON: Yeah. Oh, and that reminds me, when they say the whole plant, does include the root? Or is that just above -- the aerial part of it? I realize the aerial part is the above ground part, right?

DR. SLAGA: Right. And that's where it's cut.

MS. BURNETT: Yeah. I don't know if that means they were yanking the whole plant out of the ground, or if they're just coming with the cultivating machine and just mowing it.

And when I use just the generic term barley, it could be either species. Because the source did not define what it was, they just said barley. If I could discern it was a certain species, I would list it as such.

DR. PETERSON: So it seemed like in most of the studies you found in the literature were actually with the Vulgare version of the plant and not the dis- --

MS. BURNETT: That is the more common.

DR. PETERSON: Mm-hmm.

MS. BURNETT: And it's just how the seed head -- the seeds are placed -- organized on the head of the plant.

DR. SLAGA: Mm-hmm.

DR. PETERSON: Yeah, so I was wondering, except for the root, is it possible to read across to all the other parts? Because there's so -- you know, there's so much variability. And then I don't know if knowing that it's the whole plant, does that change the needs for -- again, I don't have huge concerns because it seems like a lot of the constituents that are in the seeds are also in the plant. You know, it's --

DR. SHANK: Right. The seed gives rise to the plant.

DR. PETERSON: Although different productions of things are going vary depending on, you know, age of the plant and growing conditions.

DR. COHEN: So you are suggesting that we possibly read across with the distichon and the Vul- -- the distichon extract, as a whole plant extract, reading across the distichon that way and the Vulgare extract -- yeah, the Vulgare extract -- as a read across for the rest of the constituents in the plant, the thing is we don't know about the root?

DR. PETERSON: Except for the root.

DR. COHEN: Yeah.

DR. PETERSON: But I didn't know how other people thought about that. I mean, that was just -- I kind of said -- these are the things I noticed, and I was so confused about what could be right and what couldn't be right. And, again, I am fairly new to this committee, you know, how I was curious how it was going to play out with everybody else. So I -- yeah, I could be pushed in either direction. But I think I'm fairly comfortable saying that you could probably read across to everything but the root.

DR. SLAGA: Well, this is the first time we're looking at it, and, to me, it would be worthwhile to see even though it's possible there's a read across. I still think that the ingredients in the root should be asked for to see if we get anything.

DR. PETERSON: Okay. And you know what else I thought would be helpful, Christina -- and I don't know if this might be an impossible task. Because I spent a fair amount of time trying to see if I could find it, but making a table with the constituents across what's -- because there is information on the seeds. There is information on the whole plant. And that, perhaps, a table sort of comparing across -- you know, the columns would be the plant part, and the rows would be the constituents. And just get a sense of the range of the constituents across the different plant parts for the data that's known.

MS. BURNETT: I can certainly --

DR. PETERSON: It would be really helpful in terms of trying to decide whether we could read across or not.

MS. BURNETT: I can certainly put that together, yes.

DR. PETERSON: Yay. Great. Because, even if it's just for us, you know, it might -- but it might be useful to have in the overall report, because it would show our logic deciding either one way or the other.

Because I did really like Table 3. It was really helpful to see, you know, how it varies. And I know Reference 29 has a similar kind of distribution for constituents. I think it's in seeds, but it's more cultivar. And it's hard to tell if there were all the Vulgare or the distichon varieties.

DR. COHEN: So are we going forward with an IDA at this point? And are we asking for more information about whether the root is involved in the entire extract? Whether other components of the leaf and root and stem water, are they food? Because that'll dictate whether we need for tox on them. Well, what else? Do I have that right? So this is an insufficient data announcement?

DR. SHANK: Yes.

DR. HELDRETH: Yes.

DR. BERGFELD: Sounds like it.

DR. HELDRETH: Procedurally, that's where the Panel typically goes with a draft report, especially on botanicals. For anything that seems insufficient or even things that seem equivocal.

DR. COHEN: Yeah.

DR. HELDRETH: This is the opportunity for the Panel to say, hey, anybody interested out there, please provide this information before we go forward.

DR. PETERSON: So I think it's worth then asking for them.

DR. COHEN: Okay. Did I leave out any?

DR. SLAGA: Yeah, that's fine for me, too.

DR. COHEN: Did I leave out anything for what we might be asking for within the IDA?

DR. SLAGA: Well, we wanted a 28 derm, and genotox, irritation -- well, 28 derm will give you if it has irritation.

DR. COHEN: For?

DR. SHANK: If they're not foods, yes.

DR. SLAGA: For the leaf ingredients and the root.

DR. COHEN: Got it. Okay. Anything else? Okay. I think next on our list is Polysilicone-11.

MS. BURNETT: Dr. Cohen?
DR. COHEN: Yes.

MS. BURNETT: Before we move on from barley --

DR. COHEN: I'm sorry.

MS. BURNETT: -- could I ask the Panel's input on some composition data we received on the seed extract? It seems to be more of what is in the trade name mixture and not actually composition data. And, if it's not informative, I don't know if the Panel wants to keep it in or to take it out.

DR. BERGFELD: Repeat what that is, Christina. Which one?

MS. BURNETT: It's under the seed extract. For those using the PDF, it would be PDF Page 12 towards the bottom.

DR. BERGFELD: Okay.

MS. BURNETT: So it would be under the --

DR. PETERSON: I thought it was helpful.

MS. BURNETT: You think that's okay too.

DR. COHEN: Why wouldn't have this been helpful?

DR. PETERSON: I guess I'm --

MS. BURNETT: It informs on the mixture, but it doesn't necessarily tell you what the composition of the seed extract is. We receive this kind of data a lot, and I just want to make sure that this is still useful.

DR. PETERSON: Are you talking about the -- it's like the third paragraph from the bottom?

MS. BURNETT: Yeah, the supplier-reported composition of a product containing three percent seed extract.

DR. PETERSON: I actually think it's helpful.

MS. BURNETT: Okay.

DR. PETERSON: I think it is because it's impurities. Basically, it's a list of impurities, right?

MS. BURNETT: Oh, yeah.

DR. COHEN: Yeah.

MS. BURNETT: Yeah. What's going into the formulation.

DR. PETERSON: Right. And you want to know what those are. And, you know, that they know, okay, they're probably innocuous, but at least you know what they are. So I actually think it's part of the impurity question.

MS. BURNETT: Okay.

DR. PETERSON: So I think it's fine, and I would leave it in, and I wouldn't take it out. I think it's important information, even though it's innocuous.

MS. BURNETT: Okay.
DR. PETERSON: But it's important because it is -- they're stating what's there and you don't have to worry about it.

MS. BURNETT: Okay. Thank you.

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DR. BELSITO: Yes, so this is the first time we're looking at these 16 botanical ingredients that are derived from barley. And, this is the only one where we got some Wave 2 data on an HRIPT of a 1.8 percent Distichon Extract. And, we felt that we needed a 28-day dermal on the whole plant extract to clear the tox endpoints, but we needed to clarify what portions of barley were GRAS. My understanding was that it was the malt and the seed, but not the other parts of the plant. But someone raised that you could eat barley grass, so we would like some further clarification on what parts of these plants are considered GRAS.

We also need sensitization, irritation, and concentration of use. I was not thrilled with the HRIPT and the 1.8 percent lotion? Because I thought that at least two panelists, panelist 8 and 10, may have had sensitization. Because they went through the entire induction phase with nothing happening, and then had some low-level reactions, a challenge, which may have certainly been due to other ingredients in the lotion. We just don't know. So I was not happy with that data that we received.

So, we're going insufficient for sensitization and irritation, 28-day dermal on the whole plant extract or clarification on what parts of the plant is considered GRAS.

DR. BERGFELD: And that is an insufficient data announcement that you're moving?

DR. BELSITO: Yes.

DR. BERGFELD: That this is a draft. Is there a second?

DR. COHEN: Second.

DR. BERGFELD: Are any other discussion points or adds to the list of needs?

DR. COHEN: I don't know if I'm adding much, but we had no data on the leaf product. We weren't sure if that was really food or not. So we wanted all the information on leaf, manufacturing, impurities, dermal tox, (inaudible) the sensitization. But we weren't clear, I think similar to what you said, Don, about the root. Is the root part of the extract? Is it only the aerial portion that's used to create the extract?

DR. BELSITO: We had that discussion as well. That, you know, Dan was under the assumption it's probably mowed and the root was not part of the extract. But we didn't know that, so I would agree we would want some further information as to where the root is involved in all of this.

DR. COHEN: Agreed.

DR. BERGFELD: About the mention of the leaf, and all the needs for the leaf. Are you going to wait on the description of what's GRAS?

DR. BELSITO: If it's GRAS we don't need it. If it's not GRAS we do.

DR. BERGFELD: Okay. All right. I'm not sure of the writer on this, but do you have a comment?

DR. COHEN: Christina.

DR. BERGFELD: Christina?

MS. BURNETT: Yes, just clarifying that the insufficient data needs are either a 28-day dermal, a tox test on a whole plant extract or clarification on the GRAS status of the leaf, stem and root ingredients, and then, sensitization and irritation data at concentration of use, which is 1.8 percent.

DR. BELSITO: For the whole extract.

MS. BURNETT: For the whole extract.

DR. BERGFELD: Anything was missed?

MS. BURNETT: Anything else?

DR. SNYDER: Well, it's 1.8 for the Distichon, and it's 1.5 for the Vulgare.

DR. BELSITO: All right, so 1.8.

MS. BURNETT: Okay.

DR. BERGFELD: Now, regarding the leaf needs, that's going to basically be based on what the GRAS classification or characterization is, correct? Okay. So this is going out as an IDA. Any other comments, adds to the discussion?

DR. SHANK: I don't think it would be a GRAS classification. GRAS is for additives.

DR. BERGFELD: Clarification. Okay.

DR. SHANK: And this is a food, not an additive.

DR. BERGFELD: Okay, so it's a food. Okay.

MS. BURNETT: So clarification --

DR. SHANK: So we need to know what's eaten and what's not eaten, but not what's on the GRAS list.

DR. BERGFELD: Okay, thank you. Anything else? Okay, I'm going to call the question on this one. It's an IDA with a long list of needs. All those opposed, please indicate by stating your name. Hearing none I'm going to say this is unanimously approved to move forward as an IDA. And our second to our last ingredient is Basic Brown 17, a hair dye, being presented by Dr. Cohen.

Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

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DRAFT ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 16 barley-derived ingredients, most of which are reported to function as skin-conditioning agents in cosmetic products. Industry should continue to use good manufacturing practices to minimize impurities that could be present in botanical ingredients. The Panel reviewed the available data to determine the safety of these ingredients. The Panel concluded (to be determined).

INTRODUCTION

The assessment of the safety of the following 16 barley-derived ingredients, as used in cosmetics, is based on the data contained in this report:

Hordeum Distichon (Barley) Extract
Hordeum Distichon (Barley) Seed Flour
Hordeum Vulgare Extract
Hordeum Vulgare Flower/Leaf/Stem Juice
Hordeum Vulgare Juice
Hordeum Vulgare Leaf Extract
Hordeum Vulgare Leaf Juice
Hordeum Vulgare Leaf Powder
Hordeum Vulgare Leaf/Stem Powder
Hordeum Vulgare Powder
Hordeum Vulgare Root Extract
Hordeum Vulgare Seed Extract
Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water
Hordeum Vulgare Sprout Extract
Hordeum Vulgare Stem Water

Hordeum distichon and *Hordeum vulgare* are two species of barley that are cultivated as a cereal grain. These two species mainly vary by the arrangement of spikelets along the central stem of the plant.[1,2] Most of barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1).[3]

The Expert Panel for Cosmetic Ingredient Safety (Panel) has reviewed the safety of Hydrolyzed Barley Protein.[4] In 2017, the Panel concluded that this ingredient is safe in cosmetics in the present practices of use and concentration in cosmetics (as described in that safety assessment). The full report on this ingredient can be accessed on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/ingredients).

Botanicals, such as barley-derived ingredients, may contain hundreds of constituents. However, in this assessment, the Panel is evaluating the potential toxicity of each botanical ingredient 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.

Many of the barley-derived seed and malt ingredients 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, the primary focus of this safety assessment is on the potential for local effects from topical exposure to these ingredients as used in cosmetics. Proteins from barley in the diet, specifically gluten, are associated with adverse health conditions (such as celiac disease) in a small portion of the general population.[5] Since the concentration of gluten in cosmetics is low, it is unlikely that enough gluten could be absorbed by the percutaneous route or by inadvertent ingestion from cosmetic products to precipitate a flare-up of either gastrointestinal or cutaneous symptoms.[6]

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that 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., *Hordeum vulgare*). Often in the published literature, the general name "barley" is used, and it is not known how the substance being tested compares to the cosmetic ingredient. Therefore, if it is not known whether the material being discussed is a cosmetic ingredient, the generic terminology, in all lowercase (e.g., barley extract or barley flour), will be used. However, if it is known that the material is a cosmetic ingredient, the naming convention provided in the *Dictionary* (e.g., Hordeum Vulgare Extract or Hordeum Vulgare Seed Flour) will be used will be used.

CHEMISTRY

Definition and Plant Identification

The definitions of the ingredients included in this review are provided in Table 1.[3] The generic CAS number for the barley ingredients in this report is 85251-64-5. Barley is the 4th most widely produced cereal grain in the world after wheat, rice, and corn.[7,8] Barley is one of the most ancient and most cultivated grains, and is more productive and stable against

seasonal variations and poor soil conditions than other grains.[1,8] The origin of *Hordeum vulgare* is uncertain, but it is believed to have been domesticated in the Fertile Crescent or in east Asia nearly 10,000 - 13,000 years ago.[1,9,10] In present day, it is cultivated on all continents, except Antarctica, in temperate and tropical areas.[11]

Table 2 lists the generic definitions of the parts of plants that are most pertinent to the ingredients in this report.[3] The barley plant is an annual grass that may be either planted in the fall (winter annual variety) or in the spring (spring annual variety).[1,12] Barley sprouts are the young leaves of barley harvested approximately 10 d after sowing seeds.[10] Stems may vary in length from 1 to 4 ft, depending on variety and growing conditions. Stem are round, hollow between nodes, and develop 5 to 7 nodes below the head. At each node, a clasping leaf develops. The spike, which contains the flowers and later the mature seeds, consists of spikelets attached to the central stem or rachis. Three spikelets develop at each node on the rachis. The barley kernel consists of the caryopsis (internal seed), the lemma (the lower bract of the floret), and palea (the upper bract of the floret). The barley kernel is generally spindle-shaped.

Hordeum vulgare L. is a 6-rowed barley with a tough rachis (spike stem) that has all florets fertile with normal kernels (i.e. all three of the spikelets at each node develop a seed).[1,2] Within this species, there are two main subgroups: a typical 6-rowed group where the lateral kernels are only slightly smaller than the central ones, and an intermedium group, where the lateral kernels are markedly smaller than the central ones.[2]

Hordeum distichon L.is a 2-rowed barley with a tough rachis comprised of a central spikelet containing a fertile flower, and lateral spikelets with male or sexless flowers (i.e. central spikelet develops a fertile flower and seed).[1,2] This species also has two main subgroups: a typical 2-rowed group with lateral florets consisting of lemma, palea, rachilla, and reduced sexual parts; and a deficiens group with reduced lateral florets consisting of lemma, palea (rarely) and rachilla, and no sexual parts.[2]

Chemical Properties

Hordeum Vulgare Seed Extract

A supplier has reported that a product that is a milky preparation of the liposoluble fraction and the water-soluble fraction of *Hordeum vulgare* seeds is an opaque, ivory-colored solution with a pH of 3.5 - 4.7.[13] A 10% diluted solution is miscible in water and alcohol 50% (v/v) and non-miscible in mineral and vegetal oils.

Another supplier has reported that Hordeum Vulgare Seed Extract is a white, odorless lyophilized powder that is stable at room temperature.[14]

Method of Manufacture

Hordeum Distichon (Barley) Extract

A supplier has reported that Hordeum Distichon (Barley) Extract is produced by extracting barley with specified eluent(s) under "appropriate temperature conditions" to yield a concentrate.[15] Typical eluents include water, butylene glycol, safflower seed oil, glycerin, and propylene glycol. The concentrate is then blended with the desired diluent(s) and preservative system to produce the final ingredient. The final ingredients are evaluated for physiochemical properties and contaminants.

Hordeum Distichon (Barley) Seed Flour and Hordeum Vulgare Seed Flour

Barley flour is milled from pearled, blocked or hull-less barley.[16] The milling system for barley is similar to that of wheat flour milling by utilizing roller mills with fluted and smooth rolls, and plansifters. Barley flour may also be a by-product of pearling and polishing processes. The methods described here are general to the processing of barley flour, and it is unknown if they apply to cosmetic ingredient manufacture.

Hordeum Vulgare Seed Extract

A supplier has reported that a tradename mixture of Hordeum Vulgare Seed Extract is obtained by decocting barley seeds with demineralized water, which is then filtered and combined with xanthan gum.[17] The same supplier reported that a product containing Hordeum Vulgare Seed Extract was obtained by combining crushed barley seeds with crushed wheat and oat seeds and performing a warm aqueous co-extraction. The resulting mixture was then combined with xanthan gum.[18]

Another supplier has reported that Hordeum Vulgare Seed Extract is produced by harvesting hydroponically cultivated barley seeds, then drying and milling them.[19] The milled seeds are then extracted with standard protein extraction buffers, containing buffering ions and sodium chloride at the appropriate pH. During this step, water-soluble barley proteins are pulled to the aqueous phase. The extract is then centrifuged to separate the slurry from the aqueous phase, which is collected for further clarification to eliminate further insoluble and unwanted particles. After clarification, the extract undergoes buffer exchange. The final steps are protein analysis, sterile filtration, and lyophilization.

Hordeum Vulgare Seed Water

A supplier has reported that Hordeum Vulgare Seed Water is obtained from dry barley seeds by steam distillate.[20] The steam distillation is carried out up to a ratio dry seed/distillate of 40%.

Composition/Impurities

Yields of constituents in barley have been found to be dependent on extraction methods and growing conditions, such as soil composition, climate, duration of growth period, and cultivar (i.e. specific genotypes, including those of different grain

colors).[21-23] Additionally, different plant parts have different constituent compositions. For example, the composition of the water-soluble flavonoid, anthocyanin, varies depending on the grain color of barley (purple, black, or yellow) and on the location of the barley grain; e.g., the anthocyanin content in the outer 10% of the bran-rich kernel layers can be as much as 6 times greater than that found in the whole kernel flour.[24] Table 3 describes the phenolic composition of three different parts of two different barley cultivars.[25] Table 4 describes the available composition information of barley-derived ingredients that is mentioned below.

In general terms, barley grain contains about 64% starch, 11% protein, and 5% β-glucan, but variation can occur through types of grain processing (e.g. pearling, milling, etc.) and plant genotype.[7,22] Phytochemicals in barley grain include phenolic acid, flavonoids (flavanols, anthocyanins, proanthocyanidins), lignans, tocols, phytosterols, and folates.[26]

Mold, yeast, and bacterial infections are the main sources of microbial contaminants in barley that may adversely affect livestock and humans that consume the harvests.[8] The main species affecting harvests are *Alternaria* spp., *Helminthosporium* spp., *Fusarium* spp., *Cladosporium* spp., *Aspergillus* spp., and *Penicillium* spp.[8] Mycotoxins produced by these fungi and bacteria may also affect barley crops; for example, barley grain can be contaminated with trichothecene 2 toxin (T-2) and its metabolite, HT-2, which are type A mycotoxins produced by fungi belonging to the genus *Fusarium,* with aflatoxins from *Aspergillus,* and naphthoquinones from *Penicillum*.[8,27,28]

Hordeum Distichon (Barley) Extract

A supplier has reported that a concentrate of Hordeum Distichon (Barley) Extract in an alcohol base had no detectable heavy metals or residual pesticides.[15] This supplier also reported that the 26 fragrance allergens defined by the European Union Cosmetic Regulations were below threshold levels for this concentrate.

Hordeum Distichon (Barley) Seed Flour and Hordeum Vulgare Seed Flour

In an analysis of whole grain flour from 12 barley cultivars, protein content ranged from 12.4% to 16.5%, free lipid content ranged from 2.0% to 2.8%, β-glucan content ranged from 4.1% to 7.4%, and polyphenols (as gallic acid) ranged from < 0.10% to 0.45%.[29] Fatty acids of barley grain flours primarily include palmitic acid (19.0% - 22.0%), stearic acid (1.1% - 1.3%), eladic acid (14.9% - 18.4%), oleic acid (0.7% - 0.8%), linoleic acid (53.6% - 57.1%), linolenic acid (4.7% - 5.7%), and eicosenoic acid (0.8% - 1.0%). Barley grain flour was determined to contain 26 volatile compounds comprising aldehydes, ketones, alcohols, and a furan (2-pentylfuran). Total volatile content was 953 - 3339 µg/l. Phenolic acids in whole grain barley flour include *p*-coumaric acid, ferulic acid, *p*-hydroxybenzoic acid, vanillic acid, caffeic acid, chlorogenic acid, protocatechuic acid, gallic acid, and syringic acid.[30]

Hordeum Distichon (Barley) Seed Flour

Acetone extracts of *Hordeum distichon* grains contain 5-*n*-alkylresorcinols.[21] Specifically, 1,3-dihydroxy-5-*n*-heneicosylbenzene (~40%); 1-3-dihydroxy-5-*n*-nonadecylbenzene (~29%); 1,3-dihydroxy-5-*n*-pentacosylbenzene (~19%); and 1,3-dihydroxy-tricosylbenzene were the predominant alkylresorcinols.

Hordeum Vulgare Juice

Phytochemical analysis of barley grass juice (15 d post-germination) was used to determine the presence of flavonoids, saponins, and terpenoids.[31] The total phenolic and flavonoid content was 225.33 mg gallic acid equivalents (GAE)/g and 203 mg quercetin equivalents/g of extract, respectively.

Hordeum Vulgare Seed Extract

Constituents of a water extract of *Hordeum vulgare* seeds included phenolics, flavonoids, anthocyanins, flavonols, tannins, triterpenoids, and vitamin C.[32] Phenolic constituents of this *Hordeum vulgare* seed extract include vanillic acid, syringic acid, vanillin, *p*-coumaric acid, ferulic acid, and ellagic acid.

In another constituent analysis of a methanol extract of *Hordeum vulgare* seeds (referred to synonymously as *Hordeum sativum*), total polyphenol content was 3.67 mg/g dry weight and total flavonoid content was 2.56 mg/g dry weight.[33] In a study of extract yields in three varieties of *Hordeum vulgare*, the total phenolic content of 100% methanol extract ranged from 88.1 to 118.5 mg/100 g extract.[34] Extracts with 80% methanol had total phenolic content ranging from 98.0 to 145.7 mg/100 g extract.

One supplier reported a tradename mixture was comprised of 3.0% Hordeum Vulgare Seed Extract, 94.9% water, 1.5% phenoxyethanol, 0.3% xanthan gum, and 0.3% potassium sorbate.[35] The same supplier reported the composition of another tradename mixture that was comprised of a 3.0% blend of Hordeum Vulgare Seed Extract, Triticum Vulgare (Wheat) Seed Extract, and Avena Sativa (Oat) Kernel Extract; 94.9% water; 1.5% phenoxyethanol; 0.3% xanthan gum; and 0.3% potassium sorbate.[36]

Another supplier has reported that the composition of a Hordeum Vulgare Seed Extract tradename mixture also contains sodium chloride and tromethamine.[14] At 1 ppm of the seed extract, there is approximately 0.038% tromethamine. No further detail on the amount of constituents was provided. Levels of the pesticides avermectin and pirimicarb were below level of detection.[37]

Hordeum Vulgare Seed Flour

Phenolic acid content of whole grain *Hordeum vulgare* flour includes caffeic acid, ferulic acid, sinapic acid, protocatechuic acid, vanillic acid, *p*-coumaric acid, *p*-hydroxybenzoic acid, syringic acid, and ferulic acid dehydrodimers.[38] The main phenolic acids were ferulic acid (250 mg/kg), ferulic acid dehydrodimers (130 mg/kg), and *p*-coumaric acid (40 mg/kg).

Hordeum Vulgare Sprout Extract

Analysis of *Hordeum vulgare* spring seedlings reported 152 phenolic secondary metabolites.[39] Flavonoids with various glycosylation and acylation, hydroxycinnamic acid glycosides, esters, and amides were identified in methanolic extracts of the leaves of nine *Hordeum vulgare* varieties. Specific derivatives included those from hordatines, hydroxyferulic acid, and flavones acylated directly on aglycone. Composition of constituents were dependent on variety, with one variety containing derivatives of flavonols, quercetin, and isorhamnetin.

An ethanol extract of *Hordeum vulgare* sprouts included the flavonoid saponarin (14.74 µg/mg), policosanol polyphenol series, various minerals (not specified), and free amino acids.[10]

The chlorophyll content of an acetone extract (10% w/v of 80%) of *Hordeum vulgare* sprouts was dependent on the age of the sprouts, with total chlorophyll content on days 7, 10, and 16 measured as 247.01 mg/100 g dry material (DM), 364.65 mg/100 g DM, and 625.20 mg/100 g DM, respectively.[40] Carotenoid content of the same extract also was dependent on the age of the sprouts, with total carotenoid content on days 7, 10, and 16 measured as 21.56 mg/100 g DM, 31.98 mg/100 g DM, and 56.08 mg/100 g DM, respectively.

Total polyphenols and total flavonoids of barley sprouts had a range of 1047.8 - 1263.2 mg GAE/100 g and 443.7 - 550.7 mg (+)-catechin hydrate equivalents/100 g DM, respectively, in four different *Hordeum vulgare* cultivars.[41] Lutonarin and saponarin were reported to be major compounds in barley sprouts, with quantities varying at different harvest times.

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, Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 167 formulations; the majority of the uses are in leave-on makeup preparations and skin care products (Table 5).[42] Hordeum Vulgare Seed Extract has the second greatest reported number of uses in this safety assessment with 36 formulations; the majority of the uses are in leave-on skin care products. The remaining 3 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council in 2018 indicate that the highest concentration of use for Hordeum Vulgare Extract is 1.5% in leave-on body and hand skin care products.[43] According to a Council survey conducted in 2020, Hordeum Distichon (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products.[44] No concentrations of use were reported for any of the other barley-derived ingredients in this report. The 11 ingredients not in use, according to the VCRP and industry survey, are listed in Table 6.[42-44]

Barley-derived ingredients may be used in products that can be incidentally ingested, come in contact with mucous membranes, or be used near the eye; for example, Hordeum Vulgare Extract is reported to be used in lipsticks at 0.15% and eye makeup preparations at up to 0.075%, and Hordeum Distichon (Barley) Extract is used at up to 0.3% in eye makeup preparations.[43,44] Additionally, some of the ingredients are used in cosmetic sprays and powders and could possibly be inhaled; for example, Hordeum Vulgare Extract is reported to be used at up to 0.03% in body and hand spray preparations, and at concentrations up to 0.015% in face powders.[43] 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.[45,46] 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.[47,48] Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[49-51]

The barley-derived ingredients described in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[52]

Non-Cosmetic

According to the US FDA, under 21 CFR 582.20, malt extract from *Hordeum vulgare* L. (or other grains) is a substance generally recognized as safe (GRAS) in animal drugs, feeds, and related products. Roughly half of the barley grown in the US

is used for livestock feed, and another quarter to a third is used for malting.[1,12] Barley for human consumption is made into pearl barley by using abrasive disks to grind the hulls and bran off the kernels.

Worldwide, barley grain is mostly used as feed for animals, malt, and food for human consumption.[8] Malt is the second largest use for barley. Barley is also grown as a hay crop in Asia, parts of the Middle East, and in northern and central Africa.[1,8]

Barley has been used in traditional medicine to treat various inflammatory and cardiovascular diseases.[53] Barley seed extract has been studied for antioxidant properties and therapeutic benefits in kidney stone and nephrotoxicity management, hepatoprotective activity against ethanol, and diabetes mellitus control and management.[32,33,54,55] Barley seed flour applied topically has been studied for therapeutic benefits in infants with jaundice.[56] Young barley grass water and juice extracts have been researched for obesity inhibition[31] and chemopreventative potential in human colon and lung cancer cell lines,[57,58] while young green *Hordeum vulgare* leaves have been studied for anti-stress properties that could be beneficial in treating psychiatric disorders such as depression.[59] Barley sprout "essence" and extract has been studied for its effects on blood cholesterol and treatment for chronic alcohol-induced liver injury.[10,60-62]

TOXICOKINETIC STUDIES

No relevant toxicokinetics studies on barley-derived ingredients were found in the public 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

Many of the barley-derived seed and malt ingredients that are addressed in this safety assessment are found in the foods that are consumed daily, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. The potential for systemic exposure from absorption of these ingredients through the skin is much less than the potential for systemic exposure from absorption through oral exposures. This is because the rates of absorption and metabolism of these ingredients in the skin are expected to be negligible compared to the corresponding rates in the digestive tract. Thus, the potential for systemic effects, other than sensitization, is not discussed in detail in this report.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

No genotoxicity toxicity studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

CARCINOGENICITY STUDIES

No carcinogenicity studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Dermal irritation and sensitization studies on barley-derived ingredients are summarized in Table 7. In human irritation tests, a product containing 0.005% Hordeum Vulgare Extract was not irritating in a 48-h patch test, while a mascara containing 0.3% Hordeum Distichon (Barley) Extract had "negligible" irritation potential in a 14-d cumulative irritation assay.[63,64] A mascara product containing 0.3% Hordeum Distichon (Barley) Extract was determined to not be sensitizing in a human repeated insult patch test (HRIPT), but low-level (±) reactions were observed in the induction and challenge phases.[65] No dermal sensitization was observed with a lotion containing 1.8% Hordeum Distichon (Barley) Extract in a HRIPT; however a slight potential for dermal irritation was noted.[66] Hordeum Distichon (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8%;[67] however, one subject had mild-moderate reactions in an HRIPT of a facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract, which may have been due to prior exposure to one of the ingredients in the test material.[68] No dermal irritation or sensitization were observed in HRIPTs of a pressed powder, a facial moisturizer, or a facial mask each containing 0.005% Hordeum Vulgare Extract, or in a skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract. [69-72]

OCULAR IRRITATION STUDIES

No ocular irritation studies for barley-derived ingredients were found in the published literature, and unpublished data were not submitted.

CLINICAL STUDIES

Ocular In-Use Studies

Horduem Distichon (Barley) Extract

The ocular irritation potential of a mascara containing 0.3% Hordeum Distichon (Barley) Extract was evaluated in an in-use study of 62 subjects.[73] Approximately a quarter of the subjects had self-perceived sensitive eyes, and more than half of the panel (47) were contact lens wearers. Subjects were instructed to apply the mascara twice daily for 4 wk. An ophthalmologist conducted slit lamp examinations at the baseline, at the 2-wk interim, and final visits. Visual acuity was measured at the initial and final visits. Questionnaires seeking subject-perceived effects were completed by the subjects at the end of each 2-wk use period. No visible clinical irritation was observed related to the use of the test material and none of the subjects reported perceived discomfort or irritation during the study period.

Hordeum Vulgare Extract

The ocular irritation potential of an eye cream containing 0.005% Hordeum Vulgare Extract was evaluated in an in-use study of 27 female subjects.[74] Approximately half of the panel had self-perceived sensitive eyes, and approximately half of the panel were contact lens wearers. After completion of a preliminary ophthalmic examination, the subjects received the test material and were instructed to use it once a day for 4 wk. At the end of the 4-wk period, the subjects underwent a comprehensive ocular examination. During the course of the exposure period, no adverse events were reported. All ophthalmologic examinations were within normal parameters. The study authors concluded that the eye cream containing 0.005% Hordeum Vulgare Extract was neither an ophthalmologic irritant in contact or non-contact lens wearers, nor in individuals with normal or self-perceived sensitive eyes.

Case Reports

Contact urticaria was reported in a 20-yr-old woman after contact with beer while working in a bar.[75] The patient presented with wheals on her hand and forearms. The wheals would appear within 15 min of exposure and would disappear after a couple hours. The patient was able to drink beer without any reactions. Skin-prick tests with wheat flour and beer were strongly positive for beer. A provocative test with beer was also positive. Specific immunoglobulin E (IgE) antibodies were detected against barley (4.33 kU/l), malt (5.13 kU/l), grass pollen (40.8 kU/l), pet dander (35 - 36 kU/l), and dust mites (> 100 kU/l). Lower levels of specific IgE antibodies (< 0.1 kU/l) were detected against wheat, rye, and oats.

A 54-yr-old malt worker at a silo presented with eczema on the fingers of both hands.[76] The patient reported that the eczema would worsen and spread to his trunk and limbs when he cleaned barley silos. Patch tests with the Portuguese standard series, fragrances, a food series, and barley and malt residues were positive (++) for barley residues (as is and in 10% petrolatum), malt radicle (as is and in 10% petrolatum), and malt residues (as is and in 10% petrolatum). A prick test to barley was negative. Serum IgE was 97.9 IU/ml.

A 23-yr-old farm laborer presented with eczema on the hands and arms.[77] A patch test of the patient was positive to barley dust. A scratch test to barley dust was negative.

OCCUPATIONAL EXPOSURES

Work-related sensitization (IgE-mediated) to barley flour and other grain dusts has been reported in bakery workers.[78-81] Commonly known as baker's asthma, reactions are often preceded by rhinitis and other respiratory symptoms, with concomitant skin symptoms such as contact urticaria and hand eczema. Atopy and sensitization to grain flour and/or enzyme (e.g., α-amylase of fungal origin) occur frequently.[78,80,81] Aside from cereal grains, baker's asthma may also be caused by molds, yeast, eggs, sesame seeds, nuts, and insects. Skin-prick testing, skin biopsies, and radioallergosorbent tests (RAST) have been utilized to identify and analyze the reactions observed in bakery workers.[78,80,81] In bakery workers with occupational asthma, RAST have shown strong associations between the levels of specific IgE to wheat flour and those of barley flour, and competitive RAST inhibition showed wheat and barley contain cross-reacting proteins.[79] Barley flour contains proteins of similar molecular weights as those in wheat (10, 52, and 69 kDa). Results of Western blotting also suggest that the cross-reacting allergens in barley have molecular weights which are similar to proteins identified as cereal α- and β-amylase, α-amylase inhibitors, trypsin and trypsin inhibitors, and protease and protease inhibitors.

EPIDEMIOLOGY OF IMMUNE-MEDIATED GLUTEN AND BARLEY REACTIONS

Celiac disease affects approximately 1% of the population worldwide, including the US, with variations between countries.[82-84] Food allergy to barley has been reported; in Korean children, evidence of cross-reactivity or co-sensitization with wheat has been found.[85,86]

SUMMARY

Hordeum distichon and *Hordeum vulgare* are two species of barley, an annual grass, that is cultivated as a cereal grain. Most of the 16 barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents. The

Panel has reviewed the safety of Hydrolyzed Barley Protein, and concluded that this ingredient is safe in cosmetics in the present practices of use and concentration.

Barley is the 4th most widely produced cereal grain in the world after wheat, rice, and corn. Barley is one of the most ancient and most cultivated grains, and is more productive and stable against seasonal variations and poor soil conditions than other grains. Yields of constituents in barley have been found to be dependent on extraction methods and growing conditions such as soil composition, climate, duration of growth period, and cultivar. Additionally, different plant parts have different constituent compositions. Barley grain may be contaminated by mycotoxins, such as aflatoxins, trichothecenes, and naphthoquinones.

According to 2021 VCRP survey data, Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 167 formulations; the majority of the uses are in leave-on makeup preparations and skin care products. Hordeum Vulgare Seed Extract has the second greatest reported number of uses in this safety assessment with 36 formulations; the majority of the uses are in leave-on skin care products. The remaining 3 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council indicate that the highest concentration of use for Hordeum Vulgare Extract is 1.5% in leave-on body and hand skin care products. Hordeum Distichon (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products. No concentrations of use were reported for the remaining 11 barley-derived ingredients in this report.

Malt extract from *Hordeum vulgare* L. or other grains is considered GRAS in animal drugs, feeds, and related products, according to the US FDA. Barley is a food grain consumed by humans and animals, and is used to malt beverages. Barley has been used in traditional medicine to treat various inflammatory and cardiovascular diseases, and its various part have been studied for treatment of numerous aliments.

Many of the barley-derived seed and malt ingredients that are reviewed in this safety assessment are found in foods consumed daily the world over. The potential for systemic exposure from the absorption of these ingredient through the skin is much less than the potential for systemic exposure from absorption through oral exposures. This is because the rates of absorption and metabolism of these ingredients in the skin are expected to be negligible compared to the corresponding rates in the digestive tract; and, the systemically available dose of these ingredients, even with theoretically complete absorption from cosmetic use, would be very small compared to that available from consumption.

In human irritation tests, a product containing 0.005% Hordeum Vulgare Extract was not irritating in a 48-h patch test, while a mascara containing 0.3% Hordeum Distichon (Barley) Extract had “negligible” irritation potential in a 14-d cumulative irritation assay. A mascara product containing 0.3% Hordeum Distichon (Barley) Extract was determined to not be sensitizing in a HRIPT, but low-level (+) reactions were observed in the induction and challenge phases. No dermal sensitization was observed with a lotion containing 1.8% Hordeum Distichon (Barley) Extract in a HRIPT; however a slight potential for dermal irritation was noted.66 Hordeum Distichon (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8%; however, one subject had mild-moderate reactions in an HRIPT of a facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract, which may have been due to prior exposure to one of the ingredients in the test material. No dermal irritation or sensitization were observed in HRIPTs of a pressed powder, a facial moisturizer, or a facial mask each containing 0.005% Hordeum Vulgare Extract, or in a skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract.

No visible clinical ocular irritation was observed related to the use of a mascara containing 0.3% Hordeum Distichon (Barley) Extract. In another in-use study, an eye cream containing 0.005% Hordeum Vulgare Extract was determined not to be an ocular irritant.

Case reports of contact urticaria and eczema have been described in patients that have been exposed to barley. Work-related sensitization has been reported in bakery workers. Celiac disease affects approximately 1% of the population worldwide. Food allergy to barley has been reported with evidence of cross-reactivity or co-sensitization with wheat.

No relevant DART studies, genotoxicity studies, carcinogenicity studies, or ocular irritation studies were found in the published literature; and unpublished data were not submitted. No relevant toxicokinetic studies were found in the published literature; however, in general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

DRAFT DISCUSSION

[Please note, this discussion is in draft form and will be modified following the meeting.]

This assessment reviews the safety of barley-derived ingredients, as used in cosmetic formulations. The Panel concluded (to be determined).

The Panel expressed concern about pesticide residues, heavy metals, and other plant species that may be present in botanical ingredients, and stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

While aflatoxin has been detected in barley grain and flour, the Panel believes that aflatoxin should not be present in barley-derived cosmetic ingredients that are derived from *Hordeum distichon or Hordeum vulgare*. The Panel has adopted the United States Department of Agriculture (USDA) designation of ≤ 15 ppb as corresponding to "negative" aflatoxin content.

Some barley-derived ingredients were reported to be used in spray and powder products that could possibly be inhaled. For example, Hordeum Vulgare Extract is reported to be used at up to 0.03% in body and hand spray preparations, and at concentrations up to 0.015% in face powders. 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 for 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. Definitions and functions of the ingredients in this safety assessment.[3]

Ingredient/CAS No.	Definition	Function
Hordeum Distichon (Barley) Extract 85251-64-5; 94349-67-4	Hordeum Distichon (Barley) Extract is the extract of the whole plant, *Hordeum distichon*.	Skin-conditioning agent – misc.
Hordeum Distichon (Barley) Seed Flour	Hordeum Distichon (Barley) Seed Flour is the flour obtained from the finely ground seeds of *Hordeum distichon*.	Abrasives; bulking agent
Hordeum Vulgare Extract 85251-64-5	Hordeum Vulgare Extract is the extract of the whole plant, *Hordeum vulgare*.	Skin-conditioning agent – misc.
Hordeum Vulgare Flower/Leaf/Stem Juice 85251-64-5	Hordeum Vulgare Flower/Leaf/Stem Juice is the juice expressed from the flowers, leaves and stems of *Hordeum vulgare.*	Skin-conditioning agent – misc.
Hordeum Vulgare Juice 85251-64-5	Hordeum Vulgare Juice is the liquid expressed from *Hordeum vulgare*.	Not reported
Hordeum Vulgare Leaf Extract 85251-64-5	Hordeum Vulgare Leaf Extract is the extract of the leaves of *Hordeum vulgare*.	Skin-conditioning agent – misc.
Hordeum Vulgare Leaf Juice 85251-64-5	Hordeum Vulgare Leaf Juice is the juice expressed from the leaf of *Hordeum vulgare*.	Skin-conditioning agent – misc.
Hordeum Vulgare Leaf Powder 85251-64-5	Hordeum Vulgare Leaf Powder is the powder obtained from the dried, ground leaves of *Hordeum vulgare*.	Skin-conditioning agent – humectant
Hordeum Vulgare Leaf/Stem Powder 85251-64-5	Hordeum Vulgare Leaf/Stem Powder is the powder obtained from the dried, ground leaves and stems of *Hordeum vulgare*.	Antioxidant
Hordeum Vulgare Powder 85251-64-5	Hordeum Vulgare Powder is the powder obtained from dried and ground whole plant, *Hordeum vulgare*.	Abrasive
Hordeum Vulgare Root Extract 85251-64-5	Hordeum Vulgare Root Extract is the extract of the roots *Hordeum vulgare*.	Skin-conditioning agent – misc.
Hordeum Vulgare Seed Extract 85251-64-5	Hordeum Vulgare Seed Extract is the extract of seeds of *Hordeum vulgare.*	Skin-conditioning agent – misc.
Hordeum Vulgare Seed Flour 85251-64-5	Hordeum Vulgare Seed Flour is the flour obtained from the finely ground seeds of *Hordeum vulgare*.	Abrasive; bulking agent
Hordeum Vulgare Seed Water 85251-64-5	Hordeum Vulgare Seed Water is the aqueous solution of the steam distillates obtained from the seeds of *Hordeum vulgare*.	Skin-conditioning agent – misc.
Hordeum Vulgare Sprout Extract 85251-64-5	Hordeum Vulgare Sprout Extract is the extract of the sprouts of *Hordeum vulgare*.	Antioxidant; skin-conditioning agent - humectant
Hordeum Vulgare Stem Water 85251-64-5	Hordeum Vulgare Stem Water is the aqueous solution of the steam distillates obtained from the stems of *Hordeum vulgare*.	Skin-conditioning agent – misc.

Table 2. Generic plant part definitions as they apply to barley-derived ingredients.[3]

Plant Part	Definition
Bran	The outer hard layers of the grain formed by the fused fruit and seed wall in grains and cereals.
Flower	The reproductive shoot in flowering plants, usually with sepals, petals, stamens and pistil(s)
Grain	Dry one-seeded fruits produced by grasses, e.g. cereals such as barley.
Hull	A dry outer covering of a fruit or seed.
Juice	The liquid contained in the vegetative parts or fruits.
Kernel	The grain of a grass.
Leaf	Flattened photosynthetic organs, attached to stems.
Root	Organ of a plant that absorbs and transports water and nutrients, lacks leaves and nodes, usually underground
Seed	A propagating sexual structure resulting from the fertilization of an ovule, formed by embryo, endosperm, or seed coat.
Sprout	Seedling; germinating seed; any new growth of a plant from a stem such as a new branch or a bud
Stem	A slender or elongated structure that supports a plant or a plant part or plant organ.

Table 3. Phenolic composition (mg/kg) of barley plant parts in 2 different cultivars.[25]

	Cultivar 1			Cultivar 2		
Phenolic Compounds	**Leaves**	**Seeds**	**Stems**	**Leaves**	**Seeds**	**Stems**
3-*O*-feruloylquinic acid	39.8	NR	5.8	4.3	NR	5.1
chlorogenic acid	NR	NR	1.1	NR	NR	0.8
lutonarin	2150.8	1.5	NR	760.8	NQ	NR
p-coumaric acid	NR	6.2	5.3	NR	3.4	18.6
isoorientin-7-*O*-rutinoside	208.4	NR	NR	68.5	NR	NR
luteolin-6-*C*-arabinoside-8-*C*-glucoside	80.5	0.3	0.9	24.6	0.2	0.4
ferulic acid	33.6	2.4	2.5	25.2	1.0	5.9
saponarin	145.3	2.0	0.3	56.4	2.4	1.2
isoorientin-7-*O*-[6-feruloyl]-glucoside-4'-*O*-glucoside AND apigenin-6-*C*-arabinoside-8-*C*-glucoside	30.9	7.3	3.4	14.2	6.4	5.4
isovitexin-7-*O*-rutinoside AND isoscoparin-7-*O*-glucoside	217.5	29.3	8.8	70.5	26.4	15.3
apigenin-6-*C*-glucoside-8-*C*-arabinoside AND isovitexin-7-*O*-[6-sinapoyl]- glucoside-4'-*O*-glucoside	14.3	0.4	NQ	7.9	0.2	NQ
isoscoparin-7-*O*-rutinoside AND isoorientin	87.6	1.7	1.1	52.3	4.5	1.5
isovitexin-7-*O*-[6-feruloyl]-glucoside-4'-*O*-glucoside	3.1	NR	NR	3.1	NR	NR
isoorientin-7-*O*-glucoside-4'-*O*-[6-feruloyl]-glucoside AND isoorientin-7-*O*-[6-caffeoyl]-glucoside AND chrysoeriol-6-*C*-glucoside-8-*C*-arabinoside AND isoscoparin-7-*O*-[6-sinapoyl]-glucoside-4'-*O*-glucoside	32.6	NR	NR	23.1	NR	NR
isoorientin-7-*O*-[6-sinapoyl]-glucoside	167.3	NR	NR	47.8	NR	NR
isoorientin-7-*O*-[6-feruloyl]-glucoside-2''-*O*-glucoside AND isoscoparin-2''-*O*-glucoside AND isovitexin	3.2	NR	NR	2.0	NR	NR
isoorientin-7-*O*-[6-feruloyl]-glucoside	494.6	NR	NR	74.8	NR	NR
isovitexin-7-*O*-[6-sinapoyl]-glucoside	18.2	NR	NR	2.5	NR	NR
isovitexin-7-*O*-[6-sinapoyl]-glucoside	27.7	NR	NR	6.0	NR	NR
Total	**3740.6**	**50.0**	**28.4**	**1232.9**	**44.4**	**51.1**

Table 4. Composition of barley-derived ingredients

Constituent	Barley Seed Flour (generic) [29,30]	Hordeum Distichon (Barley) Seed Flour[21]	Hordeum Vulgare Juice[31]	Hordeum Vulgare Seed Extract[32-34]	Hordeum Vulgare Seed Flour[38]	Hordeum Vulgare Sprout Extract[10,40,41]
Protein	12.4% - 16.5%					
Free amino acids						√
Free lipids	2.0% - 2.8%					
β-glucan	4.1% - 7.4%					
Fatty acids						
palmitic acid	19% - 22.0%					
stearic acid	1.1% - 1.3%					
eladic acid	14.9% - 18.4%					
oleic acid	0.7% - 0.8%					
linoleic acid	53.6% - 57.1%					
linolenic acid	4.7% - 5.7%					
eicosenoic acid	0.8% - 1.0%					
Vitamin C				√		
Minerals (unspecified)						√
Chlorophyll						247.01 - 625.20 mg/100 g DM (acetone)
Aldehydes	√					
Ketones	√					
Alcohols	√					
Furans	√					
Alkylresorcinols		√				
Polyphenols	<0.10% - 0.45%		Total phenolic content – 225.33 mg GAE/g	Total phenolic content – 98.0-145.7 mg/100 kg (80% methanol); 88.1-118.5 mg/100 kg (100% methanol)		Total content – 1047.8 -1263.2 mg GAE/100 g
flavonoids			Total content – 203 mg quecetin equivlaents/g	Total content – 2.56 mg/g dry weight (methanol)		Total content – 443.7-50.7 mg (+)-catechin hydrate equivalents/100 g DM
tannins				√		
tannic acid						
ellagic acid				√		
caffeic acid	√				√	
ferulic acid	√			√	250 mg/kg	
ferulic acid dehydrodimers					130 mg/kg	
sinapic acid					√	
protocatechuic acid	√				√	
vannilic acid	√			√	√	
vanillin				√		
p-coumaric acid	√			√	40 mg/kg	
p-hydroxybenzoic acid	√				√	
syringic acid	√			√	√	
gallic acid	√					
chlorogenic acid	√					
Terpenoids			√			
triterpenoids				√		
carotenoids						21.56 - 56.08 mg/100 g DM (acetone)
Saponins			√			

Table 5. Frequency (2021)[42] and concentration (2018;[43] 2020[44]) of use according to duration and type of exposure for barley-derived ingredients

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Hordeum Distichon (Barley) Extract		**Hordeum Vulgare Extract**		**Hordeum Vulgare Leaf Extract**		**Hordeum Vulgare Seed Extract**	
Totals†	**30**	**0.005-1.8**	**167**	**0.000015-1.5**	**4**	**NR**	**36**	**NR**
Duration of Use								
Leave-On	20	0.005-1.8	138	0.000015-1.5	4	NR	32	NR
Rinse Off	10	0.1	29	0.0015-0.15	NR	NR	4	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	4	0.005-0.3	4	0.005-0.075	1	NR	1	NR
Incidental Ingestion	NR	NR	16	0.15	NR	NR	NR	NR
Incidental Inhalation-Spray	8[a]; 5[b]	NR	7; 79[a]; 15[b]	0.03; 0.03-0.038[a]; 0.03[b]	3[b]	NR	12; 5[a]; 14[b]	NR
Incidental Inhalation-Powder	5[b]	0.005[c]	15[b]; 2[c]	0.015; 0.03[b]; 0.001-1.5[c]	3[b]	NR	14[b]	NR
Dermal Contact	20	0.005-1.8	148	0.000015-1.5	4	NR	36	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	10	NR	3	0.0015-0.038	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	35	0.15	NR	NR	NR	NR
Baby Products	NR	NR	2	NR	NR	NR	NR	NR

	Hordeum Vulgare Seed Flour*	
Totals†	**2**	**NR**
Duration of Use		
Leave-On	1	NR
Rinse Off	1	NR
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	NR	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	NR	NR
Incidental Inhalation-Powder	NR	NR
Dermal Contact	2	NR
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	NR	NR
Hair-Coloring	NR	NR
Nail	NR	NR
Mucous Membrane	NR	NR
Baby Products	NR	NR

NR = Not reported

† 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.

* Includes one use in the VCRP data that was listed generically as barley flour and did not distinguish species.

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

[b] Not specified whether a powder or a spray, so this information is captured for both categories of incidental inhalation.

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

Table 6. Ingredients not reported in use.[42-44]

Hordeum Distichon (Barley) Seed Flour
Hordeum Vulgare Flower/Leaf/Stem Juice
Hordeum Vulgare Juice
Hordeum Vulgare Leaf Juice
Hordeum Vulgare Leaf Powder
Hordeum Vulgare Leaf/Stem Powder
Hordeum Vulgare Powder
Hordeum Vulgare Root Extract
Hordeum Vulgare Seed Water
Hordeum Vulgare Sprout Extract
Hordeum Vulgare Stem Water

Table 7. Dermal irritation and sensitization studies for barley-derived ingredients.

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
IRRITATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	Undiluted; 0.05 ml applied	25 subjects	14-d cumulative irritation assay; occlusive patches to the same site on the upper back; patches were 15 mm diameter Webril™ discs; 0.25% sodium lauryl sulfate and a plain Webril cotton were positive and negative controls, respectively; a comparator mascara product was also tested	Test product had "negligible" irritation potential; mean cumulative irritation score was 0.24 and the cumulative irritation index was 0.01; no adverse effects of any kind were observed	64
Product containing 0.005% Hordeum Vulgare Extract	Undiluted; amount applied not reported	20 subjects	48-h patch test; occlusive patches on back; test sites examined at 15 min and 24 h post-patch removal; use of controls not reported	Not irritating; 2 subjects had an erythema score of 1 at 15 min, with 1 subject continuing with the same score at 24 h; average irritation index was 0.1 at 15 min and 0.05 at 24 h	63
SENSITIZATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	Undiluted; 0.05-0.10 g	111 subjects	HRIPT; occlusive Webril™ patches; 9 induction patches were completed over a 3-wk period and followed by a 2-wk rest period; challenge patches on previously untested sites were read 24, 48, 72, and 96 h after application	Not sensitizing; 1 subject in the induction phase and 4 other subjects in the challenge phase exhibited low-level (+) reactions	65
Lotion containing 1.8% Hordeum Distichon (Barley) Extract	Dilution status and amount applied not reported	102 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive patch on the upper back	Not a dermal sensitizer, but slight potential for eliciting dermal irritation; erythema noted during induction in several subjects and in 2 subjects during challenge phase	66
Eye cream containing 1.8% Hordeum Distichon (Barley) Extract	Undiluted; 0.2 ml	54 subjects	HRIPT conducted in a similar manner as described above; occlusive 2 cm^2 Parke-Davis Readi-Bandage®	Not irritating or sensitizing; transient, barely perceptible (0.5 level) patch responses in 10 subjects observed during either the induction or challenge phases, reactions were considered neither evidence of clinically meaningful irritation nor allergic in nature	67

Table 7. Dermal irritation and sensitization studies for barley-derived ingredients.

Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract	Dilution status not reported; 0.1-0.15 g (25-38 mg/cm^2)	49 subjects	HRIPT conducted in a similar manner as described above; occlusive Parke-Davis Readi-Bandage® patches	Not irritating or sensitizing; one subject had mild-moderate reactions during the first 3 induction patches and during challenge up to 144 h after application, response by subject was determined to be idiosyncratic and may have been due to prior exposure/sensitization to one or more components of the test material	68
Facial moisturizer containing 0.005% Hordeum Vulgare Extract	Dilution status not reported; 0.2 g	101 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive 2 cm^2 Webril™ patches	Not irritating or sensitizing; total irritation score at induction was 0	71
Facial mask containing 0.005% Hordeum Vulgare Extract	Dilution status not reported; 0.2 g	110 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive 2.54 cm^2 patch	Not irritating or sensitizing	72
Pressed powder containing 0.005% Hordeum Vulgare Extract	Dilution status and amount applied not reported; however, patches were moistened with several drop of water to ensure adherence of test material	107 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive patches	Not a dermal irritant or sensitizer	69
Skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract	Dilution status and amount applied not reported	50 subjects	HRIPT conducted in a similar manner as described above; occlusive patches	Not a dermal irritant or sensitizer; no adverse reactions were induced	70

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2021 FDA VCRP Raw Data

HORDEUM DISTICHON (BARLEY) EXTRACT	Eye Lotion	4
HORDEUM DISTICHON (BARLEY) EXTRACT	Hair Conditioner	5
HORDEUM DISTICHON (BARLEY) EXTRACT	Shampoos (non-coloring)	3
HORDEUM DISTICHON (BARLEY) EXTRACT	Tonics, Dressings, and Other Hair Grooming Aids	2
HORDEUM DISTICHON (BARLEY) EXTRACT	Other Makeup Preparations	1
HORDEUM DISTICHON (BARLEY) EXTRACT	Shaving Cream	1
HORDEUM DISTICHON (BARLEY) EXTRACT	Cleansing	1
HORDEUM DISTICHON (BARLEY) EXTRACT	Face and Neck (exc shave)	5
HORDEUM DISTICHON (BARLEY) EXTRACT	Moisturizing	2
HORDEUM DISTICHON (BARLEY) EXTRACT	Night	1
HORDEUM DISTICHON (BARLEY) EXTRACT	Skin Fresheners	2
HORDEUM DISTICHON (BARLEY) EXTRACT	Other Skin Care Preps	2
HORDEUM DISTICHON (BARLEY) EXTRACT	Other Suntan Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	Baby Lotions, Oils, Powders, and Creams	2
HORDEUM VULGARE (BARLEY) EXTRACT	Eye Lotion	3
HORDEUM VULGARE (BARLEY) EXTRACT	Other Eye Makeup Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	Other Fragrance Preparation	7
HORDEUM VULGARE (BARLEY) EXTRACT	Hair Conditioner	1
HORDEUM VULGARE (BARLEY) EXTRACT	Shampoos (non-coloring)	2
HORDEUM VULGARE (BARLEY) EXTRACT	Blushers (all types)	1
HORDEUM VULGARE (BARLEY) EXTRACT	Foundations	2
HORDEUM VULGARE (BARLEY) EXTRACT	Lipstick	16
HORDEUM VULGARE (BARLEY) EXTRACT	Makeup Bases	1
HORDEUM VULGARE (BARLEY) EXTRACT	Other Makeup Preparations	2
HORDEUM VULGARE (BARLEY) EXTRACT	Bath Soaps and Detergents	19
HORDEUM VULGARE (BARLEY) EXTRACT	Cleansing	6
HORDEUM VULGARE (BARLEY) EXTRACT	Face and Neck (exc shave)	5
HORDEUM VULGARE (BARLEY) EXTRACT	Body and Hand (exc shave)	10
HORDEUM VULGARE (BARLEY) EXTRACT	Moisturizing	74
HORDEUM VULGARE (BARLEY) EXTRACT	Night	5
HORDEUM VULGARE (BARLEY) EXTRACT	Paste Masks (mud packs)	1
HORDEUM VULGARE (BARLEY) EXTRACT	Other Skin Care Preps	9
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	Eye Lotion	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	Face and Neck (exc shave)	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	Body and Hand (exc shave)	2
HORDEUM VULGARE (BARLEY) SEED EXTRACT	Eye Lotion	1
HORDEUM VULGARE (BARLEY) SEED EXTRACT	Other Fragrance Preparation	12

HORDEUM VULGARE (BARLEY) SEED EXTRACT	Cleansing	4
HORDEUM VULGARE (BARLEY) SEED EXTRACT	Face and Neck (exc shave)	14
HORDEUM VULGARE (BARLEY) SEED EXTRACT	Moisturizing	4
HORDEUM VULGARE (BARLEY) SEED EXTRACT	Skin Fresheners	1
HORDEUM VULGARE (BARLEY) SEED FLOUR	Other Skin Care Preps	1
BARLEY FLOUR	Paste Masks (mud packs)	1

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 15, 2021

SUBJECT: Hordeum Distichon (Barley) Extract

Anonymous. 2010. A 14-day cumulative irritation assay (mascara contains 0.3% Hordeum Distichon (Barley) Extract).

Anonymous. 2010. Clinical use test (mascara contains 0.3% Hordeum Distichon (Barley) Extract).

Anonymous. 2010. Repeated insult patch test (mascara contains 0.3% Hordeum Distichon (Barley) Extract).

[redacted]

FINAL REPORT

Report Date: February 26, 2010

[redacted] Protocol: #6986

Sample: Mascara coded [redacted]

Mascara contains 0.3% Hordeum Distichon (Barley) Extract

[redacted]

E-mail address: [redacted]

[redacted]

Title: **A 14-Day Cumulative Irritation Assay**

Sponsor: [redacted]

Principal Investigator: [redacted]

Testing Facility: [redacted]

[redacted]

February 26, 2010
Date

"The names of [redacted]), any officer, employee, or collaborating scientist are not to be used for any advertising, promotional or sale purposes without the written consent of [redacted]."

FINAL REPORT

STUDY TITLE:

A 14-Day Cumulative Irritation Assay

PROTOCOL:

[redacted] #6986

GUIDELINES FOR THE CONDUCT OF THE STUDY:

All procedures were conducted in compliance with the regulations of the Food and Drug Administration (FDA) ([21CFR 50, 56, 312] ICH-GCP Consolidated Guidelines, May 9, 1997 Federal Register) and in accordance with [redacted] Standard Operating Procedures (SOP's).

SPONSOR:

[redacted]

SPONSOR STUDY:

Authorization Letter dated February 3, 2010

SPONSOR REPRESENTATIVE:

[redacted]

OBJECTIVE:

This test is designed to furnish data on the primary irritancy potential of topically applied substances in human skin.

DESIGN RATIONALE:

A repeat insult patch test study wherein the test materials were applied under occlusive dressings to designated test sites on the upper back continuously and repeatedly to the same site for a period of 14 days[2,3].

PRINCIPAL INVESTIGATOR:

[redacted]. (Board Certified Dermatologist)
Medical Director, [redacted]
[redacted]
[redacted]

[redacted] ADMINISTATIVE STRUCTURE:

[redacted]dle (Panel Recruitment/Initial Screening)
[redacted] (Patcher)
[redacted]. (Expert Grader)
[redacted] (Quality Assurance)

TESTING FACILITY:

[redacted]

DATES OF STUDY CONDUCT:

The study was conducted from February 8, 2010 through February 22, 2010.

PANEL COMPOSITION:

Healthy, normal, adult Caucasian volunteers over the age of 18 years of both sexes with no blemishes, excess hair or other marks on their upper back that would obscure grading of the test sites served as subjects.

Inclusion Criteria:

1. Healthy adult male and female volunteers between the ages of 18 and 65 years.

2. Subjects willing to follow the study requirements and provide a signed informed consent.

Exclusion Criteria:

1. History of recurrent dermatological diseases, e.g., psoriasis, atopic eczema, chronic urticaria, vitiligo, etc.
2. History of allergy or hypersensitivity to cosmetics, toiletries, or other dermatological products.
3. History of allergy or hypersensitivity to sunscreens.
4. History of allergy or hypersensitivity to any type of tape.
5. Scars, moles or other blemishes over the upper arm or back, which could interfere with the study.
6. Subjects receiving systemic or topical drugs including steroidal or non-steroidal anti-inflammatory drugs, or medications which could interfere with the development of an inflammatory response, e.g., immunosuppressive agents or retinoids
7. Subjects with any significant internal diseases, e.g., cardiac, pulmonary, renal, hepatic, etc.
8. Pregnancy or mothers who were breastfeeding or planning a pregnancy
9. Other conditions considered by the Investigator as sound reasons for disqualification from enrollment into the study.

INFORMED CONSENT:

After the protocol, reasons for the study, possible associated risks and potential benefits or risks of the treatment had been completely explained, signed, informed subject consent was obtained from each volunteer prior to the start of the study. Copies of all consent forms are on file at KGL Inc.

TEST MATERIAL:

One test sample labeled Mascara coded [redacted] (1 jar) was supplied by the sponsor and tested as supplied viz. neat (as is). The test site was also treated with 0.25% SLS (positive control) and another site was treated with plain Webril cotton

(negative control). In addition, one other test product labeled "Mascara II" and coded [redacted] was included in this panel for comparison.

HANDLING OF STUDY DOCUMENTS:

All study related documents, case report forms (CRF's), consent forms and any data generated was kept under secure lock in the technician's office during the study.

CASE REPORT FORMS:

All case report forms (CRFs) were completed in actual time during each patient's visit.

RECORDING OF DATA AND CORRECTIONS:

All data and information was recorded on specific case report forms (CRF's) and this information was recorded/or legibly printed in black ink. Any errors were crossed out with a single line and the correct entry made in ink and initialed and dated by the Investigator or by the Study Coordinator.

SUBJECT ASSIGNMENT:

Volunteer subjects were screened and qualifying subjects were selected as described above and assigned a subject number. The initials of each subject accepted into the study were recorded sequentially as they were enrolled.

METHOD AND PROCEDURES:

Approximately 0.05ml of the test material was spread uniformly onto a 15mm diameter circular disc of non-absorbing cotton cloth (Webril). The treated circular disc of Webril cotton cloth was then applied to a designated skin site measuring 15mm in diameter on the upper back. The site was then covered with occlusive tape (Blenderm, 3M) and the entire patch fastened to the skin with Scanpor Tape to ensure intimate contact with the skin. This procedure was repeated daily Mondays through Fridays with a daily fresh application of the test material for a total of 14 days. The patch remained in place over the weekends (Saturdays and Sundays). In addition to the test product and the comparator product (Mascara II coded [redacted]), one site was also treated with 0.05ml of 0.25% SLS (sodium lauryl sulfate) as a positive control and another site was treated with a plain Webril patch (cotton cloth) and served as a negative control.

ASSESSMENT AND GRADING OF RESPONSES:

Irritant reactions which may have been provoked during the study were recorded daily. All test sites were graded daily after removal of the patches for possible irritation using the following scale:

0 = normal looking skin

1 = very faint erythema with indistinct borders

2 = minimal or mild erythema with at least one discernable border

3 = moderate erythema with sharply distinct borders

4 = deep, intense erythema

5 = deep, intense erythema with edema (a palpable, raised or elevated lesion)

Other Notations: **V** = Vesicles
E = Erosions
F = Fissuring

Test sites achieving a grade 3 or greater score were discontinued and that grade (3 or 4) was carried through for the remainder of the test days for the purpose of calculating the cumulative irritation index of the test product.

RESULTS:

A total of 25 healthy Caucasian subjects who qualified were enrolled into this study. There was a total of 23 females and 2 males ranging in age from 19 to 62 years. All 25 subjects volunteers completed this investigation as outlined in [redacted]'s standard 14-Day Cumulative Irritation Assay protocol. The demography is shown in Table 1. No adverse effects of any kind were observed in any of the test panelists.

Irritation:

The individual daily and cumulative irritation scores for each test site are shown in the tables in Appendix A. The comparator product labeled Mascara II and coded [redacted]

[redacted] produced a total cumulative irritation score of "21" and a cumulative irritation index (CII) of 0.03. The test product labeled Mascara and coded [redacted] produced a total cumulative score of "6" and a CII of "0.01". By contrast, the 0.25% SLS resulted in a CII of 0.60 (severe irritation potential), while negligible irritation was seen with the plain cotton patch (a total cumulative score of "0" and a CII of 0.00). The mean irritation scores and Cumulative Irritation Indices are summarized in Table 2.

CONCLUSIONS:

The test product coded [redacted] (Mascara) was found to possess a "negligible" irritation potential in human skin while the comparator product coded [redacted] (Mascara II) was also found to possess a negligible irritation potential in human skin.

REFERENCE:

(1) Jackson, E.M.:
A Modified Cumulative Patch Test to Substantiate Hypoallergenic Claims. Cosmetic Dermatology. Vol. 7, pages 44-46, 1994.

(2) Philips, L., Steinberg, M., Maibach, H.I. and Akers, W.A.:
A Comparison of Rabbit and Human Skin Response to Certain Irritants. Toxicol.Appl.Pharmacol. 21: 369-382, 1972.

(3) Lanman, B.M., Elvers, W.B. and Howard, C.S.: The Role of Human Patch Testing in a Product Development Program. In: Proceedings, Joint Conference on Cosmetic Sciences. The Toilet Goods Association, Inc., Washington, DC, pp. 135-145, 1968.

TABLE 1

DEMOGRAPHIC DATA

Subject Number:	Subject Initials:	Age:	Sex:	Race:
01	K-S	44	F	C
02	W-W	51	F	C
03	K-V	59	F	C
04	M-P	56	F	C
05	K-T	60	F	C
06	B-B	62	F	C
07	R-M	62	M	C
08	L-A	42	F	C
09	M-O'B	21	F	C
10	A-R	61	F	C
11	M-R	39	F	C
12	S-D	20	F	C
13	J-G	36	F	C
14	J-L	58	M	C
15	K-L	31	F	C
16	M-D'C	47	F	C
17	M-L	45	F	C
18	J-P	30	F	C
19	R-S	42	F	C
20	M-N	61	F	C
21	K-T	60	F	C
22	C-S	21	F	C
23	B-F	60	F	C
24	J-T	53	F	C
25	R-P	19	F	C

C = Caucasian

TABLE 2

Mean and Cumulative Irritation Indices of Two Coded Test Products in a 14-Day Cumulative Irritation Assay

(N=25)

	TEST PRODUCTS			
	Mascara coded [redacted]	Mascara II (standard) coded [redacted]	Plain Webril	0.25% SLS
Sum of Cumulative Scores	6	21	0	450
Mean Cumulative Irritation Score	0.24	0.84	0	18.0
Mean Daily Irritation Score	0.02	0.08	0	1.80
Cumulative Irritation Index	0.01	0.03	0	0.60
Irritation Potential	Negligible	Negligible	Negligible	Severe

APPENDIX A

Cumulative Irritation Scores for Each Test Site

DAILY AND CUMULATIVE IRRITATION SCORES															
Sample: Mascara coded [redacted]															
	DAYS														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Cumulative
Subject Number	T	W	Th	F	S	S	M	T	W	Th	F	S	S	M	Score
1	0	0	0	0			0	0	0	0	0			0	0
2	0	0	0	0			0	0	0	0	0			0	0
3	0	0	0	0			0	0	0	0	0			0	0
4	0	0	0	0			0	0	0	0	0			0	0
5	0	0	0	0			0	0	0	0	0			0	0
6	0	0	0	0			0	0	0	0	0			0	0
7	0	0	0	0			0	0	0	0	0			0	0
8	0	0	0	0			0	0	0	0	0			0	0
9	0	0	0	0			0	0	0	0	0			0	0
10	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
14	0	0	0	0			0	0	0	0	0			0	0
15	0	0	0	0			0	0	0	0	0			0	0
16	0	0	0	0			0	0	0	0	0			0	0
17	0	0	0	0			0	0	0	0	0			0	0
18	0	0	0	0			0	0	0	0	0			0	0
19	0	0	0	0			0	0	0	0	0			0	0
20	0	0	0	0			0	0	0	0	0			0	0
21	0	0	0	0			0	0	0	0	0			0	0
22	0	0	0	0			0	0	0	1	1			1	3
23	0	0	0	0			0	0	0	0	0			0	0
24	0	0	0	0			0	0	0	1	1			1	3
25	0	0	0	0			0	0	0	0	0			0	0
Σ	**0**	**0**	**0**	**0**			**0**	**0**	**0**	**2**	**2**			**2**	**6**

Mean Cumulative Irritation Score:	0.24	
Mean Daily Irritation Scores:	0.02	
Cumulative Irritation Index (CII):	0.01	

DAILY AND CUMULATIVE IRRITATION SCORES															
Sample: Mascara II coded [redacted] (standard)															
	DAYS														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Cumulative
Subject Number	T	W	Th	F	S	S	M	T	W	Th	F	S	S	M	Score
1	0	0	0	0			0	0	0	0	0			0	0
2	0	0	0	0			0	0	0	0	0			0	0
3	0	0	0	0			0	0	0	0	0			0	0
4	0	0	0	0			0	0	0	0	0			0	0
5	0	0	0	0			0	0	0	0	0			0	0
6	0	0	0	0			0	0	0	0	0			0	0
7	0	0	0	0			0	0	0	0	0			0	0
8	0	0	0	0			0	0	0	0	0			0	0
9	0	0	0	0			0	0	0	0	0			0	0
10	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	1			1	2
13	0	0	0	0			0	0	0	0	0			0	0
14	0	0	0	0			0	0	1	1	1			1	4
15	0	0	0	0			0	0	0	0	0			0	0
16	0	0	0	0			0	0	0	0	0			0	0
17	0	0	0	0			0	0	1	1	1			1	4
18	0	0	0	0			0	0	0	1	1			1	3
19	0	0	0	0			0	0	0	0	0			0	0
20	0	0	0	0			0	0	0	0	0			0	0
21	0	0	0	0			0	0	0	0	0			0	0
22	0	0	0	0			0	0	0	1	2			2	5
23	0	0	0	0			0	0	0	0	0			0	0
24	0	0	0	0			0	0	0	1	1			1	3
25	0	0	0	0			0	0	0	0	0			0	0
Σ	**0**	**0**	**0**	**0**			**0**	**0**	**2**	**5**	**7**			**7**	**21**

Mean Cumulative Irritation Score:	0.84
Mean Daily Irritation Scores:	0.08
Cumulative Irritation Index (CII):	0.03

DAILY AND CUMULATIVE IRRITATION SCORES															
Sample: Plain Cotton Webril															
	DAYS														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Cumulative
Subject Number	T	W	Th	F	S	S	M	T	W	Th	F	S	S	M	Score
1	0	0	0	0			0	0	0	0	0			0	0
2	0	0	0	0			0	0	0	0	0			0	0
3	0	0	0	0			0	0	0	0	0			0	0
4	0	0	0	0			0	0	0	0	0			0	0
5	0	0	0	0			0	0	0	0	0			0	0
6	0	0	0	0			0	0	0	0	0			0	0
7	0	0	0	0			0	0	0	0	0			0	0
8	0	0	0	0			0	0	0	0	0			0	0
9	0	0	0	0			0	0	0	0	0			0	0
10	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
14	0	0	0	0			0	0	0	0	0			0	0
15	0	0	0	0			0	0	0	0	0			0	0
16	0	0	0	0			0	0	0	0	0			0	0
17	0	0	0	0			0	0	0	0	0			0	0
18	0	0	0	0			0	0	0	0	0			0	0
19	0	0	0	0			0	0	0	0	0			0	0
20	0	0	0	0			0	0	0	0	0			0	0
21	0	0	0	0			0	0	0	0	0			0	0
22	0	0	0	0			0	0	0	0	0			0	0
23	0	0	0	0			0	0	0	0	0			0	0
24	0	0	0	0			0	0	0	0	0			0	0
25	0	0	0	0			0	0	0	0	0			0	0
Σ	0	0	0	0			0	0	0	0	0			0	0

Mean Cumulative Irritation Score:	0.00
Mean Daily Irritation Scores:	0.00
Cumulative Irritation Index (CII):	0.00

DAILY AND CUMULATIVE IRRITATION SCORES															
Sample: Sodium Lauryl Sulfate (SLS) 0.25%															
	DAYS														
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Cumulative
Subject Number	T	W	Th	F	S	S	M	T	W	Th	F	S	S	M	Score
1	0	2	2	2			3	-	-	-	-			-	24
2	0	0	0	3			-	-	-	-	-			-	21
3	0	1	1	1			2	2	3	-	-			-	19
4	0	0	0	1			1	2	3	-	-			-	16
5	0	1	1	1			2	3	-	-	-			-	20
6	0	0	0	0			1	2	3	-	-			-	15
7	0	0	0	1			2	2	3	-	-			-	17
8	0	0	0	3			-	-	-	-	-			-	21
9	0	0	0	2			2	2	2	2	3			-	16
10	0	0	0	0			1	3	-	-	-			-	16
11	0	0	0	2			2	3	-	-	-			-	19
12	1	2	2	2			3	-	-	-	-			-	25
13	0	0	2	2			2	3	-	-	-			-	21
14	0	1	1	1			1	2	2	3	-			-	17
15	0	1	1	1			2	2	2	3	-			-	18
16	0	1	1	1			2	2	3	-	-			-	19
17	0	1	1	1			1	1	2	3	-			-	16
18	0	0	0	0			1	2	2	2	3			-	13
19	0	0	0	0			1	2	2	3	-			-	14
20	0	1	1	1			2	2	3	-	-			-	19
21	0	0	0	3			-	-	-	-	-			-	21
22	0	0	0	1			1	1	3	-	-			-	15
23	0	0	0	1			1	2	2	3	-			-	15
24	0	2	2	2			2	2	3	-	-			-	22
25	0	0	0	0			1	1	2	2	2			3	11
Σ	**1**	**13**	**15**	**32**			**45**	**56**	**67**	**72**	**74**			**75**	**450**

Mean Cumulative Irritation Score:	18.0
Mean Daily Irritation Scores:	1.80
Cumulative Irritation Index (CII):	0.60

STUDY REF.# TC213210

SUMMARY

Mascara contains 0.3% Hordeum Distichon (Barley) Extract

[redacted] was tested via a four-week Ophthalmologist-supervised Clinical Use study. The study was a single-blind, baseline controlled monadic design with [redacted] a Board Certified Ophthalmologist, as the principal investigator. Subjects were instructed to apply the Mascara twice daily.

The Ophthalmologist did not observe any **visible clinical irritation** related to use of [redacted].

None of the subjects using the Mascara reported a perceived discomfort/irritation response during the study period.

Claims of "Ophthalmologist Tested" and "suitable for contact lens wearers" and "suitable for sensitive eyes" are supported by the results of this study.

Reported By: [redacted]
Associate Clinical Scientist

Approved By: [redacted]
Manager

[redacted]
Consulting Ophthalmologist

STUDY REF. # TC213210

TO: [redacted] APTC-2132-10

FROM: [redacted]

DATE: August 5, 2010

SUBJECT: Clinical Use Test Results of [redacted] #[redacted]

SUMMARY

[redacted] #[redacted] was tested via a four-week Ophthalmologist-supervised Clinical Use study. The study was a single-blind, baseline controlled monadic design with [redacted] a Board Certified Ophthalmologist, as the principal investigator. Subjects were instructed to apply the Mascara twice daily.

The Ophthalmologist did not observe any **visible clinical irritation** related to use of [redacted]

None of the subjects using the Mascara reported a perceived discomfort/irritation response during the study period.

Claims of "Ophthalmologist Tested" and "suitable for contact lens wearers" and "suitable for sensitive eyes" are supported by the results of this study.

STUDY OBJECTIVES

* To determine the potential of [redacted] #[redacted] to evoke clinical irritation and/or subject-perceived discomfort/irritation when used under consumer use conditions.

* To provide support for claims of "Ophthalmologist Tested" and "suitable for contact lens wearers" and "suitable for sensitive eyes" for [redacted]

TEST DESIGN

A total of sixty-two (62) individuals completed this four-week, Ophthalmologist-supervised Clinical Use Test. In support of the claims "contact lens wearers / suitable for sensitive eyes" the current [redacted] practice requires that the test population include at least 50% contact lens wearers. In addition, the population is composed of up to 50% of individuals who consider their eyes to be sensitive, i.e. self-assessed, have allergies that affect the eyes or use sensitive eye products. In this study, forty-seven testers (76%) were contact lens wearers while the remaining fifteen did not wear contact lenses. Twenty-four percent (24%) of testers fulfilled criteria for "sensitive eyes". The Ophthalmologist conducted slit lamp examinations at the baseline, two week interim and final visits. Actual test

design and product use instructions are presented in Appendix I. Product identification is presented in Appendix II. Subject demographics are listed in the study file.

STUDY DATES

March 8, 2010 - April 12, 2010

RESULTS: OPHTHALMOLOGIST-ASSESSED VISIBLE IRRITATION

The Ophthalmologist did not observe any product related irritation. A tabulation of clinical changes may be found in Appendix III.

The Ophthalmologist observed clinical changes mainly in blepharitis, where the level of improvements was significantly higher than the level of negative changes. All other changes observed during the study period were determined to be within the parameters for normally occurring and/or seasonally related eye area conditions.

PERCEIVED IRRITATION

None of the subjects reported experiencing subjective discomfort and/or irritation during the study period.

CONCLUSION

The results of this study will provide support for claims of "Ophthalmologist Tested" and "suitable for contact lens wearers" and "suitable for sensitive eyes" for [redacted]

Prepared By: [redacted]
Associate Clinical Scientist

Approved By: [redacted]
Manager
Clinical Evaluation

cc: [redacted]

APPENDIX I

TEST DESIGN

Sixty-two (62) subjects completed a four-week, Ophthalmologist-supervised clinical use test. The panel was conducted as single-blind, baseline controlled monadic design evaluation.

The test products were supplied to all of the subjects for the 4-week evaluation period.

Test products were packaged in final packaging with final applicator and labeled with product type, i.e. MASCARA. Products were supplied to subjects with use instructions. Ophthalmologist-assessed exams of the eyes were conducted initially, at the two week interim visit, and upon completion of the study. Visual acuity was measured at the initial and final visits. Questionnaires seeking subject perceived problems were completed by the subjects at the end of each two-week use period.

TEST: [redacted]
FORMULA# [redacted]

MASCARA

APPENDIX II

USE INSTRUCTIONS
[redacted]TC-2132-10

MASCARA

USE THESE PRODUCTS **AT LEAST TWICE A DAY.**

APPLY IN THE MORNING THEN TOUCH-UP IN THE AFTERNOON OR EVENING!

USE IN PLACE OF YOUR REGULAR MASCARA

TO USE:

1. Brush upper lashes from base to tips with a long sweeping stroke. Use brush to accent lower lashes.
2. You may continue to use any of the other eye products you normally use (eyeshadow, eyeliner) but you may **not** use your normal mascara.
3. For easy removal, use soap and water or your normal choice of eye makeup removal.

REMEMBER:

1. Bring your product with you on the exam dates (March 22nd and April 12th).
2. This product is for your use only. Do not let other members of your family use it
3. Should any problems arise while using the product, please call the [redacted] and ask fo[redacted]

APPENDIX III

Total Tabulation of Clinical Changes
Ophthalmologist- Supervised
N=63*

	Test	
	#	%
# of subjects that exhibited a change**	9	15
# of subjects that exhibited no change	53	85

Blepharitis	Test
increased	1
decreased	6
Conjunctival Injection	
increased	1
decreased	0
Scaling	
increased	0
decreased	1

* - One subject dropped from the study due to non-product related reasons.

** - Subjects may have exhibited more than one change.

[redacted]

[redacted]

FINAL REPORT – REPEATED INSULT PATCH TEST (RIPT)

[redacted] **Panel #10-104**
Test Material #11B: **Mascara; Code** [redacted]

Product contains 0.3% Hordeum Distichon (Barley) Extract

PURPOSE:

To evaluate the potential of the Test Material, as a result of repeated applications, to induce dermal sensitization in human subjects.

IRB APPROVAL:

Both the [redacted] Standard Protocol #100 and the Informed Consent were approved by the Clarus Institutional Review Board (CIRB) on 1/26/10.

SPONSOR:

[redacted]

AUTHORIZATION AND SAFETY ASSURANCE:

Sponsor Authorization and Safety Assurance dated February 9, 2010.

PRINCIPAL INVESTIGATOR:
CO-INVESTIGATORS:

[redacted]

TEST FACILITY:

[redacted]

TEST MATERIAL:

Mascara; Code [redacted], a black creme, was received on February 12, 2010, with the following instructions: Test as received; apply approximately 0.05 – 0.10 gm to each patch. Allow test material to dry to the touch prior to application to skin; patch occlusively.

SUBJECTS:

The even-numbered subjects of this 200-subject panel were patched with this Test Material--123 subjects were enrolled; 111 subjects completed the test. Ten subjects discontinued due to personal reasons. Two subjects, #008 ([redacted] #35791) and #182 ([redacted] #15958), were disqualified by Quality Assurance. No subject discontinued due to test material reaction.

-CONTINUED-

[redacted]

[redacted] **Panel #10-104**
Test Material #11B: Mascara; Code [redacted]

METHOD: This test was conducted according to [redacted] Standard Protocol #100 and [redacted] Standard Operating Procedures (including any Sponsor alterations).

TEST DATES: February 17, 2010 through March 26, 2010.

SCORING SYSTEM: See Tables I-II.

RESULTS: See Tables I-II. During the Induction Phase, one subject exhibited a low-level (±) reaction

During the Challenge, four other subjects exhibited low-level (±) reactions.

CONCLUSION: In this Repeated Insult Patch Test, Mascara; Code [redacted] did not induce dermal sensitization in human subjects.

QUALITY ASSURANCE (QA): The QA Unit performed an in-phase audit of this study.

[redacted]

[redacted], MD, PhD, FAAD
Co-Investigator (Dermatologist)

[redacted], MA
Project Manager

[redacted], PhD
Principal Investigator

Date: 3/31/10

[redacted] **Panel #10-104**
Test Material #11B: **Mascara; Code** [redacted]

SUBJECTS: Each potential subject completed an [redacted] Subject History Form ([redacted] Form:SHF), including relevant medical history. (An updated Subject History Form is secured approximately every two years.) Each accepted subject was assigned a permanent [redacted] Identification Number. No subject was used if he or she exhibited any dermatological or other medical or physical condition that would preclude topical application of the Test Material. No subject reported using any medication that would interfere with sensitization results. No known pregnant nor nursing women were used on this RIPT. No minor subjects were used on this RIPT.

An appropriate clearance period had elapsed since a subject was patched on a Repeated Insult Patch Test (RIPT) or a Photoallergy Test (PA) before being used in this RIPT.

Legally valid written IRB-approved Informed Consent, in conformity with: 21 CFR 50.25, Subtitle A, Protection of Human Subjects, was secured from each subject.

METHOD: Induction Phase: A webril/adhesive patch (Kendall Healthcare Products Company Patch #4022), or equivalent, was used occlusively. Approximately 0.05 – 0.10 gm of the Test Material was applied to each patch. As per [redacted] Standard Operating Procedures (SOP) ([redacted] Form:SOP/RIPT), the left side of the back was usually the test area for the Induction Phase. The subject's skin was marked with gentian violet surgical marker at the left side of the test site. The test site was recorded on the anatomical diagram of each subject's individual Data Form. In addition, at this time, the prospective placement of the Challenge test site was also recorded on the anatomical diagram.

Each subject was instructed that the patch was to remain in place and kept dry for approximately 24 hours, at which time the patch was to be removed by the subject. A 24-hour period, during which no test material was applied, followed the weekday patch removals; a 48-hour period followed the weekend patch removals.

Each subject returned to [redacted] on the appropriate day. The test site was observed by the [redacted] technician, and the reaction scored and recorded (see **SCORING SYSTEM**, below). The identical test site was then repatched until the nine Induction patchings were completed.

In accordance with [redacted] SOP, if a subject was unable to make up a missed patching during the same week, the subject was either patched four days the following week or was patched at the end of the Induction Phase. Any absences and make-up days are noted by the dates on the individual Data Form.

A series of nine (9) Induction patchings was completed over a period of approximately three weeks.

Rest Period: A Rest Period of approximately two weeks followed the last Induction patching; no test material was applied during the Rest Period.

[redacted]

[redacted] **Panel #10-104**
Test Material #11B: **Mascara; Code** [redacted]

METHOD: (continued)

Challenge Phase: At the Challenge Phase, the original Induction test site was observed and each subject queried as to whether any reaction was experienced during the Rest Period. A webril/adhesive patch (Kendall Healthcare Products Company Patch #4022), or equivalent, was used occlusively. Approximately 0.05 – 0.10 gm of the Test Material was applied to each patch. As per [redacted] RIPT SOP, the right side of the back was usually the virgin test site for the Challenge Phase.

As per [redacted] RIPT SOP, the Challenge patch was applied to the virgin site only. Each subject was again instructed to keep the patch on and dry.

Each subject reported to [redacted] approximately 24 hours later (Challenge Reading 1), at which time the patch was removed and the Challenge site scored and recorded by the [redacted] technician. The original test site was also observed. (See **RESULTS**, below.)

Each subject reported to HRL at approximately 48 hours (Challenge Reading 2), approximately 72 hours (Challenge Reading 3) and approximately 96 hours (Challenge Reading 4) post-patching for additional observations; reactions were scored and recorded.

Four subjects, #038 ([redacted] #35875), #072 ([redacted] #33455), #074 ([redacted] #35093) and #172 ([redacted] #20195), missed Challenge Reading 4. All of the subjects returned to [redacted] on March 29, 2010 and their test sites were negative. A verbal report from each of these subjects stated 'no reaction present' at what would have been his or her Challenge Reading 4.

SCORING SYSTEM: See Tables I-II. The test sites were scored using the modified scoring scale of the International Contact Dermatitis Research Group System: Fisher, Alexander A., *Contact Dermatitis*, Lea & Febiger, Philadelphia, 1986: p 26.

RESULTS: See Tables I-II. No serious adverse events related to the Test Material occurred during this test. Erythema, edema, dryness, staining, peeling and hyperpigmentation are possible, expected endpoints and not considered Adverse Reactions. This test was conducted under the supervision of a Board-Certified Dermatologist, a Co-Investigator. At Challenge Reading 3, the Dermatologist participated in the scoring of the subjects. A total of 111 subjects completed the test; 34 male and 77 female. The subjects range in age from 18 to 77.

RETENTION: All original Data Forms will be retained at [redacted] for a period of three years, or such other time as may be required by law. A laboratory retainer bottle of the Test Material shall be retained, in ambient conditions, for at least two years, or as required by law. Return or disposal of unused Test Material shall be as per the Sponsor's instructions—to be communicated within 30 days of receipt of this Final Report. [redacted] shall appropriately dispose of any Test Material after six months if no Sponsor instructions have been communicated.

[redacted]

[redacted]
[redacted] Panel #10-104
Test Material #11B: **Mascara; Code** [redacted]

TABLE I: SUMMARY OF REACTIONS

TOTAL NUMBER OF SUBJECTS ENROLLED: 123
TOTAL NUMBER OF SUBJECTS COMPLETED: 111

Reaction	Induction Reading									Challenge Reading			
Grade	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**1**	**2**	**3**	**4**
0	121	120	117	116	114	113	112	111	111	111	109	107	105
±		1	1								2	3	2
1													
1E													
2													
2E													
3													
4													
-												1	4
N9R													
Total	**121**	**121**	**118**	**116**	**114**	**113**	**112**	**111**	**111**	**111**	**111**	**111**	**111**

SCORING SYSTEM:

0	No visible reaction
±	Faint, minimal erythema
1	Erythema
2	Intense erythema, induration
3	Intense erythema, induration, vesicles
4	Severe reaction with erythema, induration, vesicles, pustules (may be weeping)
E	Edema
-	No reading
N9R	No 9th reading

[redacted]

[redacted] Panel #10-104
Test Material #11B: **Mascara; Code** [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
002	32282	KM	F	52	0	0	0	0	0	0	0	0	0	0	0	0	0
004	35807	TB	M	28	0	0	0	0	0	0	0	0	0	0	0	0	0
006	30295	CS	F	50	0	0	0	0	0	0	0	0	0	0	0	0	0
008	35791	CP	F	41	0	0	0	0	0	0	0	X	X	X	X	X	X
010	33531	SP	F	52	0	0	0	0	0	0	0	0	0	0	±	±	±
012	30149	VG	F	49	0	0	0	0	0	0	0	0	0	0	0	0	0
014	35878	MB	F	54	0	0	0	0	0	0	0	0	0	0	0	±	±
016	34314	CC	M	67	0	0	0	0	0	0	0	0	0	0	0	0	0
018	27367	EM	F	27	0	0	0	0	0	0	0	0	0	0	0	0	0
020	32810	LI	F	47	0	0	0	0	0	0	0	0	0	0	0	0	0
022	35292	NG	F	48	0	0	0	0	0	0	0	0	0	0	0	0	0
024	34761	DH	F	52	0	0	0	0	0	0	0	0	0	0	0	0	0
026	27723	NG	F	30	0	0	0	0	0	0	0	0	0	0	0	0	0
028	30923	TK	F	47	0	0	0	0	0	0	0	0	0	0	0	0	0
030	23640	ND	M	64	0	0	0	0	0	0	0	0	0	0	0	0	0
032	30230	GG	M	45	0	0	0	0	0	0	0	0	0	0	0	0	0
034	23125	RM	M	27	0	0	X	X	X	X	X	X	X	X	X	X	X
036	33279	EG	F	55	0	0	0	0	0	0	0	0	0	0	0	0	0
038	35875	ML	F	20	0	0	0	0	0	0	0	0	0	0	0	0	-
040	28424	SG	M	64	0	0	0	0	0	0	0	0	0	0	0	0	0
042	33790	BW	M	55	0	0	0	0	0	0	0	0	0	0	0	0	0
044	35547	AG	F	22	0	0	0	0	0	0	0	0	0	0	0	0	0
046	29261	JM	F	45	0	0	0	0	0	0	0	0	0	0	0	0	0
048	24354	ED	M	64	0	0	0	0	0	0	0	0	0	0	0	0	0
050	22643	JL	F	29	0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted] Panel #10-104
Test Material #11B: **Mascara; Code** [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	**HRL**	**Ini**	**Sex**	**Age**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**1**	**2**	**3**	**4**
052	35882	VS	F	19	0	0	0	0	0	0	0	0	0	0	0	0	0
054	34777	SG	M	63	0	0	0	0	0	0	0	0	0	0	0	0	0
056	13864	MP	M	69	0	0	0	0	0	0	0	0	0	0	0	0	0
058	34693	KK	F	52	0	0	0	0	0	0	0	0	0	0	0	0	0
060	35798	CG	F	21	0	0	X	X	X	X	X	X	X	X	X	X	X
062	35797	LZ	F	46	0	0	0	0	0	0	0	0	0	0	0	0	0
064	35079	RR	M	59	0	0	0	0	0	0	X	X	X	X	X	X	X
066	32914	IR	F	32	0	0	0	0	0	0	0	0	0	0	0	0	0
068	34264	MH	F	55	0	0	0	0	0	0	0	0	0	0	0	0	0
070	35853	EA	M	26	X	X	X	X	X	X	X	X	X	X	X	X	X
072	33455	AN	F	36	0	0	0	0	0	0	0	0	0	0	0	0	-
074	35093	NS	F	26	0	0	0	0	0	0	0	0	0	0	0	0	-
076	35888	KR	F	18	0	0	0	0	0	0	0	0	0	0	0	0	0
078	34654	VQ	F	63	0	0	0	0	0	0	0	0	0	0	0	0	0
080	34191	DC	M	44	0	0	0	0	0	0	0	0	0	0	0	0	0
082	27116	ZG	F	23	0	0	0	0	0	0	0	0	0	0	0	0	0
084	35828	LM	M	23	0	0	0	0	0	0	0	0	0	0	0	0	0
086	22128	JD	M	27	0	0	0	0	0	0	0	0	0	0	0	0	0
088	34278	MC	F	30	0	0	0	0	0	0	0	0	0	0	0	0	0
090	35892	NR	F	61	0	0	0	0	0	X	X	X	X	X	X	X	X
092	29967	AR	F	30	0	0	0	0	0	0	0	0	0	0	0	0	0
094	17270	CP	F	49	0	0	0	0	0	0	0	0	0	0	0	0	0
096	33096	MI	F	68	0	0	0	0	0	0	0	0	0	0	0	0	0
098	35842	EO	M	27	0	0	0	0	0	0	0	0	0	0	0	0	0
100	24864	JO	F	37	0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted] Panel #10-104
Test Material #11B: **Mascara; Code** [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	**HRL**	**Ini**	**Sex**	**Age**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**1**	**2**	**3**	**4**
102	27403	LS	F	50	0	0	0	0	0	0	0	0	0	0	0	0	0
104	35755	ER	F	42	0	0	0	0	0	0	0	0	0	0	0	0	0
106	32077	PM	F	19	0	0	0	0	0	0	0	0	0	0	0	0	0
108	34118	MB	F	51	0	0	0	0	0	0	0	0	0	0	0	0	0
110	33257	MV	F	45	0	0	0	0	0	0	0	0	0	0	0	0	0
112	35835	KB	F	49	0	±	±	X	X	X	X	X	X	X	X	X	X
114	32343	GC	F	53	0	0	0	0	0	0	0	0	0	0	0	0	0
116	32885	LL	M	52	0	0	0	0	0	0	0	0	0	0	0	0	0
118	31618	SB	F	53	0	0	0	0	0	0	0	0	0	0	0	0	0
120	27675	KA	F	36	0	0	0	0	0	0	0	0	0	0	0	0	0
122	29837	JA	M	22	0	0	0	0	0	0	0	0	0	0	0	0	0
124	32342	MM	F	36	0	0	0	0	0	0	0	0	0	0	0	0	0
126	34365	SG	F	34	0	0	0	0	0	0	0	0	0	0	0	0	0
128	31145	SB	F	30	0	0	0	0	0	0	0	0	0	0	0	0	0
130	26579	TR	F	48	0	0	0	0	0	0	0	0	0	0	0	0	0
132	34535	BB	F	48	0	0	0	0	0	0	0	0	0	0	0	0	0
134	29041	MC	F	38	0	0	0	0	0	0	0	0	0	0	0	0	0
136	35817	JG	M	27	0	0	0	0	0	0	0	0	0	0	0	-	0
138	32525	DW	M	41	0	0	0	0	0	0	0	0	0	0	0	0	0
140	33466	JS	M	18	0	0	0	0	0	0	0	0	0	0	0	0	0
142	25327	LC	F	37	0	0	0	0	0	0	0	0	0	0	0DR	±DR^	0DR^
144	29505	CR	M	49	0	0	0	0	0	0	0	0	0	0	0	0	0
146	32558	DR	F	48	0	0	0	0	0	0	0	0	0	0	0	0	0
148	34992	DS	F	57	X	X	X	X	X	X	X	X	X	X	X	X	X
150	29040	RC	F	46	0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted]
[redacted] Panel #10-104
Test Material #11B: Mascara; Code [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	HRL	Ini	Sex	Age	1	2	3	4	5	6	7	8	9	1	2	3	4
152	35868	SL	F	29	0	0	X	X	X	X	X	X	X	X	X	X	X
154	30580	NT	F	30	0	0	0	0	0	0	0	0	0	0	0	0	0
156	35871	MS	F	67	0	0	0	0	0	0	0	0	0	0	0	0	0
158	18616	BC	F	50	0	0	0	0	0	0	0	0	0	0	0	0	0
160	30780	JC	M	46	0	0	0	0	0	0	0	0	0	0	0	0	0
162	24390	AL	F	49	0	0	0	0	0	0	0	0	0	0	0	0	0
164	32838	KM	M	43	0	0	0	0	0	0	0	0	0	0	±	0	0
166	35479	FV	M	45	0	0	0	0	0	0	0	0	0	0	0	0	0
168	35550	DR	F	20	0	0	0	0	0	0	0	0	0	0	0	0	0
170	35903	DH	F	41	0	0	0	0	0	0	0	0	0	0	0	0	0
172	20195	GG	M	42	0	0	0	0	0	0	0	0	0	0	0	0	-
174	31987	RF	M	35	0	0	0	0	0	0	0	0	0	0	0	0	0
176	27612	AR	F	39	0	0	0	0	0	0	0	0	0	0	0	0	0
178	35873	AM	F	55	0	0	0	0	0	0	0	0	0	0	0	0	0
180	35874	LO	M	39	0	0	0	0	0	0	0	0	0	0	0	0	0
182	15958	PV	F	25	0	0	0	X	X	X	X	X	X	X	X	X	X
184	35409	RS	F	66	0	0	0	0	0	0	0	0	0	0	0	0	0
186	35084	LP	F	31	0	0	0	0	0	0	0	0	0	0	0	0	0
188	30165	MF	F	64	0	0	0	0	0	0	0	0	0	0	0	0	0
190	35507	LC	F	31	0	0	0	0	0	0	0	0	0	0	0	0	0
192	34730	HA	M	52	0	0	0	0	0	0	0	0	0	0	0	0	0
194	15112	JB	M	48	0	0	0	0	0	0	0	0	0	0	0	0	0
196	17358	JM	M	62	0	0	0	0	0	0	0	0	0	0	0	0	0
198	28119	HL	F	35	0	0	0	0	X	X	X	X	X	X	X	X	X
200	16853	ZT	F	55	0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted] Panel #10-104

Test Material #11B: **Mascara; Code** [redacted]

TABLE II: INDIVIDUAL SUBJECT DATA

(see Scoring System, page 11)

					Induction Reading									Challenge Reading			
Sub	**HRL**	**Ini**	**Sex**	**Age**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**1**	**2**	**3**	**4**
202	21482	KS	F	65	0	0	0	0	0	0	0	0	0	0	0	0	0
204	22424	IV	F	53	0	0	0	0	0	0	0	0	0	0	0	0	0
206	35674	EQ	F	58	0	0	0	0	0	0	0	0	0	0	0	0	0
208	31626	XZ	F	45	0	0	0	0	0	0	0	0	0	0	0	0	0
210	26644	GC	F	58	0	0	0	0	0	0	0	0	0	0	0	0	0
212	32192	RM	F	44	0	0	0	0	0	0	0	0	0	0	0	0	0
214	35398	WZ	M	62	0	0	0	0	0	0	0	0	0	0	0	0	0
216	30661	AG	M	46	0	0	0	0	0	0	0	0	0	0	0	0	0
218	35397	CF	F	59	0	0	0	0	0	0	0	0	0	0	0	0	0
220	09276	JR	F	51	0	0	0	0	0	0	0	0	0	0	0	0	0
222	35774	LC	M	32	0	0	0	0	0	0	0	0	0	0	0	0	0
224	32471	EB	F	77	0	0	0	0	0	0	0	0	0	0	0	0	0
226	35790	DR	F	48	0	0	0	0	0	0	0	0	0	0	0	0	0
228	30962	HV	M	48	0	0	0	0	0	0	0	0	0	0	0	0	0
230	29100	TH	F	25	0	0	0	0	0	0	0	0	0	0	0	0	0
232	35480	JA	M	40	0	0	0	0	0	0	0	0	0	0	0	0	0
234	20617	BB	F	59	0	0	0	0	0	0	0	0	0	0	0	0	0
236	35777	KR	F	20	0	0	0	0	0	0	0	0	0	0	0	0	0
238	21946	YD	F	42	0	0	0	0	0	0	0	0	0	0	0	0	0
240	35911	SP	F	27	0	0	0	0	X	X	X	X	X	X	X	X	X
242	30020	BR	M	37	0	0	0	0	0	0	0	0	0	0	0	0	0
244	23007	BW	F	47	0	0	0	0	0	0	0	0	0	0	0	0	0
246	29127	EC	F	47	0	0	0	0	0	0	0	0	0	0	0	0	0

[redacted]

[redacted] Panel #10-104
Test Material #11B: **Mascara; Code** [redacted]

SCORING SYSTEM*:

0	No visible reaction
±	Faint, minimal erythema
1	Erythema
2	Intense erythema, induration
3	Intense erythema, induration, vesicles
4	Severe reaction with erythema, induration, vesicles, pustules (may be weeping)
E	Edema
DR	Dryness
^	Hyperpigmentation
ST	Staining
P	Peeling
C	Change of test site
-	No reading
N9R	No 9th reading
X	Discontinued

*International Contact Dermatitis Research Group System: Fisher, Alexander A., *Contact Dermatitis*, Lea & Febiger, Philadelphia, 1986: p 26

[redacted]

[redacted]
[redacted] **Panel #10-104**
Test Material #11B: **Mascara; Code** [redacted]

QUALITY ASSURANCE MEMORANDUM

This Final Report was reviewed for accuracy and conformity with both [redacted] Standard Protocol #100 and [redacted] Standard Operating Procedures (including any Sponsor alterations) and any written communication form the Sponsor.

Inspections were accomplished by a random sampling approach and reported to the Project Manager and the Principal Investigator immediately following their completion.

The raw data for this study are retained at [redacted]

[redacted]

[redacted]

[redacted]

Quality Assurance Manager

QUALITY ASSURANCE UNIT

Dated: 3/31/10

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 2, 2021

SUBJECT: Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract

Essex Testing Clinic, Inc. 2010. Repeated insult patch test (facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract).

Reliance Clinical Testing Services, Inc. 2008. Human repeated insult patch test (eye cream containing 1.8% Hordeum Distichon (Barley) Extract).

TKL Research. 2015. Repeated insult patch test study (facial moisturizer containing 0.005% Hordeum Vulgare Extract).

Consumer Product Testing Co. 2016. Repeated insult patch test (facial mask containing 0.005% Hordeum Vulgare Extract).

Essex Testing Clinic, Inc.

ETC

FINAL REPORT

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

facial moisturizer contains 2.76%
Hordeum Distichon (Barley) Extract

[redacted]

Sponsor

[redacted]

Sponsor Representative

[redacted]

Clinical Testing Facility

Essex Testing Clinic, Inc.
799 Bloomfield Avenue
Verona, NJ 07044

Sponsor Code: T28
ETC Panel No.: 09354
ETC Entry No.: 17793
[redacted]

Date of Final Report

1-25-10

ETC Panel No.: 09354
ETC Entry No.: 17793

SIGNATURE PAGE

CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

Susan Russnak
Assistant Project Manager
Study Director

20 January 2010
Date

Toni F. Miller, PhD, DABT, BCFE
Scientific Director
Principal Investigator

20 January 2010
Date

John A. Erianne, MD
Board-Certified Dermatologist
Medical Investigator

1/22/10
Date

Essex Testing Clinic, Inc.

QUALITY ASSURANCE STATEMENT

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in CFR Title 21, Parts 50, 56 and 312 and/or the Declaration of Helsinki, as appropriate.

For purposes of this clinical study:

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

This study report has been reviewed to assure that it correctly describes the methods of testing and that the reported results accurately reflect the data obtained during the clinical study (ETC Panel No.: 09354; ETC Entry No.: 17793).

Sherri L. Sayles, MS
Manager, Quality Assurance

22 Jan 2010
Date

ETC Panel No.: 09354
ETC Entry No.: 17793

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CLINICAL SAFETY EVALUATION

REPEATED INSULT PATCH TEST

[redacted]

1.0 OBJECTIVE

The objective of this study was to determine the irritation and/or sensitization potential of the test article after repeated application under occlusive patch test conditions to the skin of human subjects (non-exclusive panel).

2.0 SPONSOR

[redacted]

2.1 Sponsor Representative

[redacted]

3.0 CLINICAL TESTING FACILITY

The study was conducted by:

Essex Testing Clinic, Inc.
799 Bloomfield Avenue
Verona, NJ 07044

4.0 CLINICAL INVESTIGATORS

Principal Investigator:	Toni F. Miller, PhD, DABT, BCFE
Medical Investigator:	John A. Erianne, MD, Board-Certified Dermatologist
Study Director:	Susan Russnak

5.0 STUDY DATES

Study initiation: December 2, 2009

Final evaluation: January 8, 2010

6.0 ETHICS

6.1 Ethical Conduct of the Study

This study was conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and/or Essex Testing Clinic (ETC) Standard Operating Procedures.

6.2 Subject Information and Consent

This study was conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed Consent was obtained from each subject in the study and documented in writing before participation in the study. A copy of the Informed Consent was provided to each subject.

7.0 TEST MATERIAL

The test article used in this study was provided by:

[redacted]

It was received on November 25, 2009 and identified as follows:

ETC Entry No.	Test Article I.D.	Description
17793	[redacted]	Off- White Cream

8.0 TEST SUBJECTS

At least 50 male and female subjects ranging in age from 18 to 79 years were to be empanelled for this test.

The subjects chosen were to be dependable and able to read and understand instructions. The subjects were not to exhibit any physical or dermatologic condition that would have precluded application of the test article or determination of potential effects of the test article.

9.0 TEST PROCEDURE

The 9 Repeated Insult (occlusive) Patch Test (9-RIPT) was conducted as follows:

9.1 Induction Phase

A sufficient amount of the test article (approximately 0.1 g – 0.15 g) was placed onto a Parke-Davis Readi-Bandage® occlusive patch (approximately 25 - 38 mg/cm^2 of test material) and applied to the back of each subject between the scapulae and waist, adjacent to the spinal mid-line. This procedure was performed by a trained technician/examiner and repeated every Monday, Wednesday and Friday until 9 applications of the test article had been made.

The subjects were instructed to remove the patch 24 hours after application. Twenty-four hour rest periods followed the Tuesday and Thursday removals and 48-hour rest periods followed each Saturday removal. Subjects returned to the Testing Facility and the site was scored by a trained examiner just prior to the next patch application.

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

9.2 Challenge Phase

After a rest period of approximately 2 weeks (no applications of the test article), the Challenge patch was applied to a previously unpatched (virgin) test site. The site was scored 24 and 72 hours after application. All subjects were instructed to report any delayed skin reactivity that occurred after the final Challenge patch reading. When warranted, selected test subjects were called back to the Clinic for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

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

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

All other observed dermal sequelae (eg, edema, dryness, hypo- or hyperpigmentation) were appropriately recorded on the data sheet and described as mild, moderate or severe.

9.0 TEST PROCEDURE (CONT'D)

9.3 Data Interpretation

Edema, vesicles, papules and/or erythema that persist or increase in intensity either during the Induction and/or Challenge phase may be indicative of allergic contact dermatitis. Allergic responses normally do not resolve or improve markedly at 72-96 hours.

Exceptions to typical skin reactions may occur. These may include, but not be limited to, symptoms of allergic contact sensitivity early in the Induction period to one or more test products. When this occurs in one subject, such a reaction usually suggests either an idiosyncratic response or that the subject had a pre-exposure/sensitization to the test material or component(s) of the test material or a cross-reactivity with a similar product/component. Data for such reactions will be included in the study report but will not be included in the final study analysis/conclusion of sensitization.

10.0 RESULTS AND DISCUSSION

(See Table 1 for Individual Scores)

A total of 55 subjects (8 males and 47 females ranging in age from 18 to 68 years) were empanelled for the test procedure. Forty-nine (49/55) subjects satisfactorily completed the test procedure on Test Article: [redacted] Six (6/55) subjects discontinued for personal reasons unrelated to the conduct of the study. Discontinued panelist data are shown up to the point of discontinuation, but are not used in the Conclusions section of this final report.

Induction Phase Summary

Test Article	Induction Scores (Number of Responses)						Evidence of Clinically Significant Irritation
	0.5	1	2	3	4	Other	
[redacted]	0	1	2	0	0	0	No

Challenge Phase Summary

Test Article	Challenge Scores (Number of Responses)						Evidence of Sensitization
	0.5	1	2	3	4	Other	
[redacted]	0	1	2	0	0	0	No

One subject (Subject No. 8) exhibited a moderate (level 2) response at the first Induction evaluation. The patch site was changed. Another mild (level 1) response was exhibited at the second Induction evaluation followed by a moderate (level 2) response with severe drying at the third Induction evaluation. Further Induction patching was discontinued for this subject. The same subject had a moderate (level 2) response at the 24- and 72-hour Challenge evaluations. At the 144-hour evaluation, there was a mild (level 1) response.

10.0 RESULTS AND DISCUSSION (CONT'D)

Based on the lack of response on any other subjects, the response on Subject No. 8 is judged to be idiosyncratic and may be indicative of prior exposure/sensitization to one or more components of the test article. Therefore, the response is not considered to represent a clinically significant response for the overall population.

11.0 CONCLUSIONS

Under the conditions of a repeated insult (occlusive) patch test procedure conducted in 49 subjects, Test Article: [redacted] was "Dermatologist-Tested" and was not associated with clinically significant skin irritation or allergic contact dermatitis in human subjects.

ETC Panel No.: 09354
ETC Entry No.: 17793

TABLE 1

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj. No.	Induction Evaluation Number									Challenge Virgin Site	
	1	2	3	4	5	6	7	8	9	24hr	72hr
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0
8	2c	1	2d	-	-	-	-	-	-	2	2(144hr=1)
9	0	0	0	0	0	0	0	0	0	0	0
10	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
14	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0	0	0
19	Discontinued										
20	Discontinued										
21	0	0	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0

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

c = change of patch site
d = severe drying
- = no patch application

ETC Panel No.: 09354
ETC Entry No.: 17793

TABLE 1 (CONT'D)

INDIVIDUAL SCORES

REPEATED INSULT PATCH TEST - OCCLUSIVE

Test Article: [redacted]

Subj. No.	Induction Evaluation Number									Challenge Virgin Site	
	1	2	3	4	5	6	7	8	9	24hr	72hr
31	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	Discontinued							
36	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	Discontinued			
42	0	0	0	0	0	0	0	0	0	0	0
43	0	Discontinued									
44	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0
53	0	0	Discontinued								
54	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0

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

Reliance Clinical Testing Services, Inc.
3207 Esters Road
Irving, TX 75062
Phone 972-871-7578 Fax 469-524-0714

RCTS, INC. *"Your Assurance for Quality in Clinical Testing"*

FINAL REPORT
RCTS' STUDY NO. 2404
TRA PROJECT NUMBER: 99001-196
HUMAN REPEATED INSULT PATCH TEST (HRIPT)

Sponsor:	[redacted] eye cream containing 1.8% Hordeum Distichon (Barley) Extract		
Sponsor's Representative:	[redacted]		
Sponsor's Test Article Code:	[redacted]	**RCTS' Test Article Code:**	2404.2839
Testing Facility:	RCTS, Inc. 3207 Esters Road Irving, TX 75062		
Study Objective:	To determine the irritation and sensitization potential of a test article under occlusive patch test conditions after repeated applications to the skin of approximately fifty (50) human subjects.		
Method:	Modified HRIPT Draize Procedure Induction: Occlusive patches applied on the back 3 times each week for 3 weeks. Patches worn for approximately 24-hours and removed, unsupervised, by the subject. Rest phase: 10-17 days. Challenge: One 24-hour patch on a virgin/naïve test site. Skin Evaluations: Induction evaluation occurred: Approximately 24- to 48-hours after patch removal. Challenge evaluation occurred: Approximately 24- and 72-hours after patch application (i.e., immediately after patch removal and again 48 hours after patch removal. Additional readings were made, if warranted).		
Number of Subjects:	Fifty-four (54) subjects satisfactorily completed the test procedure.		
Panel Description:	Male and female subjects aged 22 to 64 years successfully completed the test procedure.		
Conclusions:	☒ Non-sensitizing ☐ Sensitizing ☐ Additional data needed	☒ Non-irritating ☐ Irritation acceptable (normal) for product type ☐ Irritation higher than normal for product type	
Study Start Date:	28-May-2008	**Study End Date:**	03-July-2008
Document Status:	Final	**Date:**	24-July-2008

Barry T. Reece, M.S., M.B.A.
Principal Investigator
Vice President/Managing Partner

7/24/08
Date of Final Report

Raymond L. Garcia, M.D.
Medical Investigator
Board Certified Dermatologist

Dorsi R. Simmons, B.S.
Study Coordinator
Manager, Clinical Research Coordinator

QUALITY ASSURANCE STATEMENT

This study was conducted in accordance with the spirit of Good Clinical Practice regulations described in CFR 21, Part 50 (Protection of Human Subjects - Informed Consent), Part 56 (Institutional Review Boards) and the International Conference on Harmonization – Good Clinical Practice Guidelines, May 9, 1997, Federal Register.

For Purposes of this clinical study:

- ☒ Informed Consent was obtained.
- ☐ Informed Consent was not obtained.
- ☒ An IRB review was neither requested nor required.
- ☐ An IRB was convened and approval to conduct the proposed clinical research was granted.

The Quality Assurance Department conducted in-study inspections (audits) on a random sampling of subjects during the study. Written status reports of the inspections and findings were submitted to Management.

Date of Inspection	Type of Inspection	Date Reported to Management
05/28/2008	Day 1 procedures including study organization and management, qualification of subjects, consenting process and patching procedures.	05/28/2008
06/04/2008 06/11/2008 06/18/2008	Induction phase procedure including patching procedures and scoring of the test sites.	06/04/2008 06/11/2008 06/18/2008
06/30/2008	Day 1 of Challenge phase procedure including patch application and explanation of Challenge procedure to the subject.	06/30/2008
07/01/2008	24-Hour observation of Challenge phase.	07/02/2008
07/03/2008	72-Hour observation of Challenge phase.	07/03/2008
07/17/2008	Final Review of Data Tables	07/17/2008
07/22/2008	Review of Draft Report	07/22/2008
07/24/2008	Review of Final Report	07/24/2008

This study report has been reviewed to ensure that it correctly describes the methods of testing and that the reported results accurately reflect the data obtained during the clinical study (RCTS' Study No. 2404; RCTS' Test Article Code: 2404.2839).

On the basis of the audits conducted, this report is considered to be a true and accurate reflection of the methods of testing and source data obtained.

Rachel Blackwell — 7-24-08

Rachel Blackwell, B.S.
Quality Assurance

Date

Samatha Prema. M.S — 07/24/08

Samatha Prema. M.S
Quality Assurance

Date

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APPENDIX

Clinical Safety Evaluation
Human Repeated Insult Patch Test (HRIPT)

1. SUMMARY

A Modified Draize procedure[1] was conducted to determine the potential of **Test Article:** [redacted] to induce irritation and contact sensitization in a population of normal, healthy subjects.

Of the sixty-nine (69) subjects enrolled in the study, fifty-four (54) subjects satisfactorily completed the test procedure. Seven (7) test subjects (Subject Nos.: 29, 32, 37, 40, 49, 55 and 60) were discontinued due to noncompliance (e.g., either excessive missed visits or unwillingness to follow procedures outlined in protocol). One (1) test subject (Subject No. 44) was discontinued due to tape reaction (tape dermatitis). Seven (7) test subjects (Subject Nos.: 1, 4, 7, 31, 56, 64 and 65) could not be contacted to determine the reason for discontinuation; therefore, these subjects were considered "lost to follow-up".

Under the conditions of a Human Repeated Insult Patch Test Procedure (Modified Draize; occlusive patch conditions), [redacted] produced transient, barely perceptible (0.5-level) patch test responses (specific and non-specific) on ten (10/54) test subjects during either the Induction or Challenge phase of the study. The skin reactivity observed was considered neither evidence of clinically meaningful irritation nor allergic in nature.

2. OBJECTIVE

To determine the irritation and sensitization potential of a test article under occlusive patch test conditions after repeated applications to the skin of approximately fifty (50) human subjects.

3. INVESTIGATORS

Principal Investigator: Barry T. Reece, M.S., M.B.A.
Medical Investigator: Raymond L. Garcia, M.D. (Board Certified Dermatologist)
Study Coordinator: Dorsi R. Simmons, B.S.

4. SPONSOR

[redacted]

5. SPONSOR'S REPRESENTATIVE

[redacted]

6. TESTING FACILITY

The study was conducted at and by RCTS, Inc. at 3207 Esters Road, Irving, TX 75062.

7. EXPERIMENTAL DESIGN

7.1 INFORMED CONSENT

The investigator (or his designee) explained the nature of the study, its purpose and associated procedures, the expected duration and the potential benefits and risks of participation to each subject prior to his/her entry into the study. Each subject was provided with a copy of the informed consent form, had ample opportunity to ask questions and was informed about the right to withdraw from the study at any time without any disadvantage and without having to provide reasons for this decision. No subject entered the study before his/her informed consent form was obtained.

---

[1] Draize, J.H., Woodard, G. and Calvery, H.D.: Methods for the study of irritation and toxicity of substances applied topically to the skin and mucous membranes. Journal of Pharmacology and Experimental Therapeutics 83, 377-390, 1944.

7.2 SUBJECT SELECTION

Sixty-nine (69) subjects, 40 females and 29 males, ranging in age from 18 to 64 years were empanelled in this study.

7.2.1 INCLUSION CRITERIA

Subjects included in the study:

1. Were male and female volunteers between the ages of eighteen (18) and seventy (70), in general good health based upon a study screener (no physical required);
2. Were of any skin type or ethnicity, provided their degree of skin pigmentation did not significantly interfere with evaluations;
3. Were free of any systemic or dermatological disorder including a known history of allergies or other medical conditions which, in the opinion of the investigator, might have interfered with the conduct of the study, interpretation of results or increased the risk of adverse reactions;
4. Agreed to refrain from swimming, using hot tubs/saunas and any type of tanning;
5. Were able to read, understand and provide written informed consent; and
6. Agreed to complete the course of the study and to comply with instructions.

7.2.2 EXCLUSION CRITERIA

Subjects excluded from the study:

1. Were women who were pregnant, nursing or planning to become pregnant during the course of the study;
2. Were individuals with any visible dermatological condition that might have interfered with evaluations;
3. Were individuals with abnormal skin pigmentation at the test sites that might have interfered with subsequent evaluations of dermal responsiveness;
4. Were individuals who were taking medications that might have interfered with the test results, including any regimen of steroidal/non-steroidal anti-inflammatory drugs or antihistamines;
5. Were individuals with a known history of allergies to cosmetics, personal care products or fragrances;
6. Were individuals who were under treatment for asthma or diabetes; and/or
7. Were individuals who were enrolled in a study or had participated in a patch test study within 14 days prior to the start of this study.

7.2.3 SUBJECT DEMOGRAPHICS

Demographic information is summarized in Text Table 7-1.

Of the 69 subjects who were enrolled, 58.0% were female and 42.0% were male. Additionally, 39.1% were African American, 33.3 % Caucasian, 26.1% Hispanic and 1.4% Native American. Subjects' ages ranged from 18-64 years. The mean age of the subjects enrolled in the study was 41.8 years with a standard deviation of 12.1 years. The age range of females was 18-64 years. The mean age of females enrolled in the study was 42.3 years with a standard deviation of 12.4 years. The age range of males was 22-60 years. The mean age of males who were enrolled in the study was 41.0 years with a standard deviation of 11.9 years.

Of the sixty-nine (69) subjects enrolled in the study, fifty-four (54) subjects satisfactorily completed the test procedure. Seven (7) test subjects (Subject Nos.: 29, 32, 37, 40, 49, 55 and 60) were discontinued due to noncompliance (e.g., either excessive missed visits or unwillingness to follow procedures outlined in protocol). One (1) test subject (Subject No. 44) was discontinued due to tape reaction (tape dermatitis). Seven (7) test subjects (Subject Nos.: 1, 4, 7, 31, 56, 64 and 65) could not be contacted to determine the reason for discontinuation; therefore, these subjects were considered "lost to follow-up".

Of the 54 subjects who completed the study, 57.4% were female and 42.6% were male. Additionally, 38.9% were African American, 37.0 % Caucasian and 24.1% Hispanic. Subjects' ages ranged from 22-64 years. The mean age of the subjects who completed the study was 43.7 years with a standard deviation of 11.8 years. The age range of females was 22-64 years. The mean age of females who completed the study was 44.6 years with a standard deviation of 11.4 years. The age range of males was 22-60 years. The mean age of males who completed the study was 42.6 years with a standard deviation of 12.4 years.

Text Table 7-1 Demographics of Subjects

		Enrolled N=69	Completed N=54
Age of Test Subjects (years)	Mean	41.8	43.7
	SD	12.1	11.8
	Median	42.0	45.0
	Range	18-64	22-64
Gender of Test Subjects	Female	40 (58.0%)	31 (57.4%)
	Male	29 (42.0%)	23 (42.6%)
Ethnicity	African American	27 (39.1%)	21 (38.9%)
	Caucasian	23 (33.3%)	20 (37.0%)
	Hispanic	18 (26.1%)	13 (24.1%)
	Native American	1 (1.4%)	0 (0.0%)

Discontinued subjects' data are shown, up to the point of discontinuation, but are not used in the Results and Discussion or Conclusions sections of this final report.

7.3 TEST ARTICLE

The test article was provided by [redacted] The test article was received on May 27, 2008 and identified as follows:

Text Table 7-2 Test Article Information

Sponsor's Test Article Code	RCTS' Test Article Code	Manufacturer	Description	Identity
[redacted]	2404.2839	[redacted]	Off-white cream	Personal Care Product

*Tested neat (as received).

The testing facility confirmed receipt of the test article and used the test article only within the framework of this clinical study and in accordance with the study protocol. Responsibility of the identity, purity, strength, composition and stability of the test article remained with the sponsor. The test article was stored at room temperature in a secured location until use.

8. METHOD

The Human Repeated Insult Patch Test (HRIPT) was conducted as follows:

8.1 INDUCTION PHASE

The Induction phase was initiated on May 28, 2008.

8.1.1 Screening/Induction 1/Day 1

At the Screening/Day 1 visit, potential subjects received all necessary written and verbal information and signed an informed consent form prior to entering the study. Subjects who fulfilled all of the inclusion and none of the exclusion criteria outlined in the study protocol were allowed to participate in the study and received a unique subject number.

Prior to test article application the test site was evaluated to ensure no dermatological condition, or anything that would interfere with the evaluation of the test site, was present. The site was initially wiped with a cotton ball treated with 70% isopropyl alcohol after which approximately 0.2 mL, or enough to cover the entire patch, of the test article was placed onto a 2 cm x 2 cm occlusive patch (Parke-Davis Readi Bandage, Kendall Healthcare, Mansfield, MA, USA) and the patch applied to the back of each subject above the waist, between the left scapula and the spinal mid-line. The test article was tested neat (as received). The subjects were instructed to remove the patch 24-hours after application.

8.1.2 Inductions 2-9/Days 3-20

On Days 3-20, subjects arrived at the testing facility at which time they were queried as to any adverse events they may have experienced or any concomitant medications they may have taken since their last visit to the testing facility. The test site was then scored by a trained evaluator just prior to the next patch application using the following 6-point scale:

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

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

Following evaluation, the test site was cleansed with a cotton ball wet with 70% isopropyl alcohol and a fresh patch of the test article was applied to the subject's back. The subjects were instructed to remove the patch 24-hours after application. In general, this procedure was repeated every Monday, Wednesday and Friday until nine (9) applications of the test article had been made. A twenty-four (24) hour rest period followed the Tuesday and Thursday removals and a 48-hour rest period followed each Saturday removal.

Procedurally, if a subject developed a 2-level (moderate) erythema reaction or greater during the Induction phase, or if the skin responses warranted a change in site, the patch was applied to a previously unpatched, adjacent site. If a 2-level reaction (or greater) occurred at the new site, no further applications were made; however, all subjects were subsequently patched with the test material at a naïve site during the Challenge phase of the study unless, in the opinion of the Principal Investigator, it was unwise to do so.

8.1.3 Day 22 (read only)

On Day 22 subjects returned to the testing facility and a trained evaluator examined the test site and recorded the degree of erythema and any other dermal sequelae present. At the conclusion of the Day 22 visit no further patches were applied and the subjects began a 10-17 day rest period following the final Induction application.

8.2 CHALLENGE PHASE

The Challenge phase was initiated on June 30, 2008. The final Challenge patch reading was made on July 03, 2008.

8.2.1 Day 1 of Challenge Phase

Approximately 10-17 days following the application of the last Induction patch subjects returned to the testing facility for the Challenge phase of the study. The same test article evaluated in the Induction phase was applied in the Challenge phase under the same testing conditions. Application consisted of applying the test article to a patch and applying the patch to a naïve site located away from the original application site (opposite side of the upper back). During the challenge phase the test article remained in contact with the skin for a period of approximately 24 hours.

8.2.2 Days 2 and 4 of Challenge Phase (24 and 72 hours after patch application)

Subjects returned to the testing facility twenty-four (24) hours after Challenge patch application for supervised patch removal. The site was scored 24- and 72-hours after test article application (i.e., immediately after patch removal and again 48-hours after patch removal) using the same 6-point scale as used for the Induction phase. All subjects were instructed to report any delayed skin reactivity that might have occurred after the final Challenge patch reading. When warranted, selected test subjects returned to the testing facility for additional examinations and scoring to determine possible increases or decreases in Challenge patch reactivity.

9. PROTOCOL AMENDMENTS

No amendments were made to the original protocol.

10. ADVERSE EVENTS (AEs)

No adverse events were reported during the course of the study.

11. PROTOCOL DEVIATIONS

No protocol deviations were recorded during the course of the study.

12. CHANGES IN THE CONDUCT OF THE STUDY

There were no changes in the conduct of the study.

13. RESULTS AND DISCUSSION

(See Post-Text Table I for Individual Scores)

Transient, barely perceptible (0.5-level) patch test responses (specific and non-specific) were observed on ten (10/54) test subjects [Subject Nos.: 6, 9, 14, 20, 26, 38, 58, 67, 68 and 69] during either the Induction or Challenge phase of the study. The skin reactivity observed was considered neither evidence of clinically meaningful irritation nor allergic in nature. A summary table for the frequency of clinical observations for the Induction and Challenge phases is shown below:

Frequency Table

Clinical Score:	Induction Exposure No.									Challenge	
	1	2	3	4	5	6	7	8	9	24 Hr	72 Hr
0	50	54	53	53	54	54	54	54	52	52	54
0.5	4	0	1	1	0	0	0	0	2	2	0
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
Total	54	54	54	54	54	54	54	54	54	54	54

14. CONCLUSIONS

Under the conditions of a Human Repeated Insult Patch Test Procedure (Modified Draize; occlusive patch conditions), **Test Article:** [redacted] produced transient, barely perceptible (0.5-level) patch test responses (specific and non-specific) on ten (10/54) test subjects during either the Induction or Challenge phase of the study. The skin reactivity observed was considered neither evidence of clinically meaningful irritation nor allergic in nature.

[redacted]

Subjects' Individual Scores

Subj. No.	Subj. Init.	Subj. Age	Subj. Gender	Subj. Ethnicity	Induction Exposure No.									Challenge Reading (Hrs)	
					1	2	3	4	5	6	7	8	9	24	72
1	ZW	38	Male	African American	Disc										
2	NL	59	Male	African American	0	0	0	0	0	0	0	0	0	0	0
3	VW	46	Female	African American	0	0	0	0	0	0	0	0	0	0	0
4	DW	26	Female	African American	0	0	0	Disc							
5	LV	49	Male	African American	0	0	0	0	0	0	0	0	0	0	0
6	RD	45	Male	African American	0	0	0	0	0	0	0	0	0.5	0	0
7	RG	26	Male	Hispanic	0	0	0	0	Disc						
8	NH	60	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
9	BD	30	Male	Caucasian	0.5	0	0	0	0	0	0	0	0	0	0
10	RH	47	Female	African American	0	0	0	0	0	0	0	0	0	0	0
11	PM	45	Female	African American	0	0	0	0	0	0	0	0	0	0	0
12	TE	41	Female	African American	0	0	0	0	0	0	0	0	0	0	0
13	NJ	24	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
14	KW	46	Male	African American	0	0	0	0	0	0	0	0	0	0.5	0
15	AS	32	Female	African American	0	0	0	0	0	0	0	0	0	0	0
16	LH	23	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
17	WS	29	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
18	BS	30	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
19	MF	48	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
20	GV	57	Male	Hispanic	0	0	0	0.5	0	0	0	0	0	0	0
21	MR	53	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
22	CH	28	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
23	SH	64	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
24	DW	22	Male	African American	0	0	0	0	0	0	0	0	0	0	0
25	BC	58	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
26	JG	51	Female	Caucasian	0	0	0	0	0	0	0	0	0.5	0	0
27	MJ	43	Female	African American	0	0	0	0	0	0	0	0	0	0	0
28	DI	57	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
29	CM	46	Female	Caucasian	Disc										
30	SM	38	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
31	SB	28	Female	African American	0	Disc									
32	ND	33	Female	African American	0	0	0	0	0	Disc					
33	DR	43	Male	Hispanic	0	0	0	0	0	0	0	0	0	0	0
34	RJ	55	Female	African American	0	0	0	0	0	0	0	0	0	0	0
35	KS	33	Female	African American	0	0	0	0	0	0	0	0	0	0	0
36	SN	26	Male	African American	0	0	0	0	0	0	0	0	0	0	0
37	PT	34	Male	African American	0	Disc									
38	SB	39	Male	Caucasian	0	0	0.5	0	0	0	0	0	0	0	0
39	AJ	42	Female	African American	0	0	0	0	0	0	0	0	0	0	0
40	LS	48	Male	Native American	Disc										

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

Disc = Discontinued

[redacted]

Post-Text Table 1
RCTS' Study No. 2404
HRIPT (Occlusive)

Subjects' Individual Scores

Subj. No.	Subj. Init.	Subj. Age	Subj. Gender	Subj. Ethnicity	Induction Exposure No. 1	2	3	4	5	6	7	8	9	Challenge Reading (Hrs) 24	72
41	JG	53	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
42	MB	42	Female	African American	0	0	0	0	0	0	0	0	0	0	0
43	AP	42	Male	Hispanic	0	0	0	0	0	0	0	0	0	0	0
44	AM	37	Male	Hispanic	0	0	0	Disc							
45	LM	39	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
46	BL	22	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
47	JG	26	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
48	BD	47	Male	African American	0	0	0	0	0	0	0	0	0	0	0
49	DP	28	Male	Caucasian	0.5	Disc									
50	GS	60	Male	African American	0	0	0	0	0	0	0	0	0	0	0
51	CW	39	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
52	SE	56	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
53	DH	51	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
54	TL	42	Female	Caucasian	0	0	0	0	0	0	0	0	0	0	0
55	SG	33	Female	Hispanic	Disc										
56	HM	56	Female	Hispanic	Disc										
57	JT	59	Male	Hispanic	0	0	0	0	0	0	0	0	0	0	0
58	JW	59	Female	Caucasian	0	0	0	0	0	0	0	0	0	0.5	0
59	MT	45	Female	Hispanic	0	0	0	0	0	0	0	0	0	0	0
60	CG	22	Female	Hispanic	0	0	0	0	0	0	Disc				
61	MH	50	Male	Caucasian	0	0	0	0	0	0	0	0	0	0	0
62	RP	42	Male	African American	0	0	0	0	0	0	0	0	0	0	0
63	MB	52	Female	African American	0	0	0	0	0	0	0	0	0	0	0
64	KH	49	Female	African American	0	0	0	Disc							
65	BA	18	Female	Caucasian	0	Disc									
66	EK	39	Female	African American	0	0	0	0	0	0	0	0	0	0	0
67	AB	49	Male	Caucasian	0.5	0	0	0	0	0	0	0	0	0	0
68	SS	23	Male	Caucasian	0.5	0	0	0	0	0	0	0	0	0	0
69	JM	61	Female	Caucasian	0.5	0	0	0	0	0	0	0	0	0	0

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

Disc = Discontinued

Frequency Table

Clinical Score:	Induction Exposure No. 1	2	3	4	5	6	7	8	9	Challenge 24 Hr	72 Hr
0	50	54	53	53	54	54	54	54	52	52	54
0.5	4	0	1	1	0	0	0	0	2	2	0
1	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0
Total	54	54	54	54	54	54	54	54	54	54	54

REPEATED INSULT PATCH STUDY

TKL STUDY NO. DS101515

Product Identification Number: ENG075488, P.S. 1-64.1B

facial moisturizer contains 0.005% Hordeum Vulgare Extract

CONDUCTED FOR:

[redacted]

DATE OF ISSUE:

April 24, 2015

TABLE OF CONTENTS

APPENDICES

SIGNATURES

This study was conducted in compliance with the requirements of the protocol and TKL's Standard Operating Procedures, and in the spirit of GCP ICH Topic E6.[1] The report accurately reflects the raw data for this study.

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Jonathan S. Dosik, MD
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Michelle Medina
Manager, Dermatologic Safety Testing

April 24, 2015
Date

STATEMENT OF QUALITY CONTROL

The Quality Control Unit of the Dermatological Safety Department conducted a 100% review of all study-related documents. The protocol was reviewed prior to the start of the study, and the medical screening forms and informed consent documents were reviewed in-process of the study. The regulatory binder and study data were reviewed post-study to ensure accuracy. The study report was reviewed and accurately reflects the data for this study.

[1] ICH Topic E6 "Note for guidance on Good Clinical Practices (CPMP/ICH/135/95)" – ICH Harmonised Tripartite Guideline for Good Clinical Practices having reached Step 5 of the ICH Process at the ICH Steering Committee meeting on 1 May 1996.

TITLE OF STUDY

Repeated Insult Patch Study

SPONSOR

[redacted]

STUDY MATERIAL

Crème, ENG075488, P.S. 1-64.1B

DATE STUDY INITIATED

March 2, 2015

DATE STUDY COMPLETED

April 10, 2015

DATE OF ISSUE

April 24, 2015

INVESTIGATIVE PERSONNEL

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One Promenade Boulevard, Suite 1101
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SUMMARY

One product, ENG075488, P.S. 1-64.1B, was evaluated neat to determine its ability to sensitize the skin of volunteer subjects with normal skin using a semi-occlusive repeated insult patch study. Naïve skin served as a negative control and 0.1% SLS served as a positive control. One hundred one (101) subjects completed Induction and were evaluable for irritation and 101 subjects completed the study and were evaluable for sensitization. The study product, ENG075488, P.S. 1-64.1B achieved a total irritation score of 0, compared to 406 for the positive control.

Under the conditions employed in this study, there was no evidence of significant irritation or sensitization to product, ENG075488, P.S. 1-64.1B.

1.0 OBJECTIVE

The objective of this study was to determine the ability of the study material to cause irritation and/or sensitization by repeated topical applications to the skin of humans under controlled patch study conditions.

2.0 RATIONALE

Substances that come into contact with human skin need to be evaluated for their propensity to irritate and/or sensitize. Once an appropriate pre-clinical safety evaluation has been performed, a reproducible, standardized, quantitative patch evaluation procedure must be used to demonstrate that a particular material can be applied safely to human skin without significant risk of adverse reactions. The method herein employed is generally accepted for such a purpose.

Repeated insult patch evaluation is a modified predictive patch study that can detect weak sensitizers that require multiple applications to induce a cell-mediated (Type IV) immune response sufficient to cause an allergic reaction. Irritant reactions may also be detected using this evaluation method, although this is not the primary purpose of this procedure. Results are interpreted according to interpretive criteria based upon published works, as well as the clinical experience of TKL Research, Inc. These interpretive criteria are periodically reviewed and amended as new information becomes available.

3.0 STUDY DESIGN

3.1 STUDY POPULATION

A sufficient number of subjects were enrolled to provide 100 completed subjects. In the absence of any sensitization reactions in this sample size (100 evaluable subjects), a 95% upper confidence bound on the population rate of sensitization would be 3.5%.

3.1.1 Inclusion Criteria

Individuals eligible for inclusion in the study were those who:

1. Were males or females, 18 to 75 years of age, inclusive;
2. Were free of any systemic or dermatologic disorder which, in the opinion of the investigative personnel, would have interfered with the study results or increased the risk of adverse events (AEs);
3. Were of any skin type or race, providing the skin pigmentation would allow discernment of erythema;
4. Had completed a medical screening procedure; and
5. Had read, understood, and signed an informed consent (IC) agreement.

3.1.2 Exclusion Criteria

Individuals excluded from participation in the study were those who:

1. Had any visible skin disease at the study site which, in the opinion of the investigative personnel, would have interfered with the evaluation;

2. Were receiving systemic or topical drugs or medication which, in the opinion of the investigative personnel, would have interfered with the study results;
3. Had psoriasis and/or active atopic dermatitis/eczema;
4. Were females who were pregnant, planning to become pregnant during the study, or breast-feeding; and/or
5. Had a known sensitivity to cosmetics, skin care products, or topical drugs as related to the material being evaluated.

3.1.3 Informed Consent

A properly executed IC document was obtained from each subject prior to entering the study. The signed IC document is maintained in the study file. In addition, the subject was provided with a copy of the IC document (see Appendix III).

3.2 DESCRIPTION OF STUDY

3.2.1 Outline of Study Procedures

Subjects participated in the study over a 6-week period involving 3 phases: (1) Induction, (2) Rest, and (3) Challenge. Prior to study entry, the subjects were screened to assure that they met the inclusion/exclusion criteria. Informed consent was obtained. Each subject was provided with a schedule of the study activities. All subjects were told to avoid wetting the patches and were asked not to engage in activities that caused excessive perspiration. They were instructed to notify the staff if they experienced any discomfort beyond mild itching or observed any adverse changes at the patch sites, while on the study or within 2 weeks of completing the study.

The Induction Phase consisted of 9 applications of the study material and subsequent evaluations of the patch sites. Prior to application of the patches, the sites were outlined with a skin marker, eg, gentian violet. Patches were applied on Mondays, Wednesdays, and Fridays for 3 consecutive weeks. The subjects were required to remove the patches approximately 24 hours after application. They returned to the facility at 48-hour intervals to have the sites evaluated and identical patches applied to the same sites. Patches applied on Friday were removed by subjects after 24 hours. The sites were evaluated on the following Monday, ie, 72 hours after patch application.[2]

Following the 9th evaluation, the subjects were dismissed for a Rest Period of approximately 10-15 days.

Subjects who were absent once during the Induction Phase received a make-up (MU) patch at the last Induction Visit. The MU applications were graded 48 hours later at the MU visit, or were recorded as N9G (no ninth grading). Subjects who missed the 9th evaluation (N9G) but have had 9 patch applications were considered to have completed the Induction Phase.

The Challenge Phase was initiated during the sixth week of the study. Identical patches were applied to sites previously unexposed to the study material. The patches were removed by subjects after 24 hours and the sites graded after additional 24-hour and 48-hour periods (ie, 48 and 72 hours after application). Following a negative Induction, a 48/72-hour sequence of "0/2," "1/2," or "2/2"

[2] A Monday or Friday holiday could result in evaluation at 96 hours after patch application.

resulted in an additional reading being performed at the 96-hour interval. Rechallenge was performed whenever there was evidence of possible sensitization.

To be considered a completed case, a subject must have had 9 applications and no fewer than 8 subsequent readings during Induction, and a single application and 2 readings at Challenge. Only completed cases were used to assess sensitization.

3.2.2 Study Flow Chart

WEEK 1

DAY	ACTIVITIES
1[3]	Staff obtained informed consent, reviewed completed medical screening form, applied patches
2	Subject removed patches
3	Staff graded sites, applied patches
4	Subject removed patches
5	Staff graded sites, applied patches
6	Subject removed patches

WEEK 2

1	Staff graded sites, applied patches
2-6	Same as Week 1

WEEK 3

1-6	Same as Week 2

WEEK 4

1	Staff graded sites; applied make-up (MU) induction patches, if required
2	Subject removed MU induction patches
3	Staff graded MU induction sites at MU visit
2-7	Rest Period

WEEK 5

1-7	Rest Period

WEEK 6

1	Staff applied patches
2	Subject removed patches
3	Staff graded sites
4	Staff graded sites

[3] Study flow starting with Week 1, Day 1, will be altered when enrollment occurs other than on Monday. Study flow could be altered when a holiday occurs during the study.

3.2.3 Definitions Used for Grading Responses

The symbols found in the scoring scales below were used to express the response observed at the time of examination:

0 = No reaction

1 = Minimal or doubtful response, slightly different from surrounding normal skin

2 = Definite erythema, no edema

3 = Definite erythema, definite edema

4 = Definite erythema, definite edema and vesiculation

SPECIAL NOTATIONS

E = Marked/severe erythema

S = Spreading of reaction beyond patch site (ie, reaction where material did not contact skin)

p = Papular response > 50%

pv = Papulovesicular response > 50%

D = Damage to epidermis: oozing, crusting and/or superficial erosions

I = Itching

X = Subject absent

PD = Patch dislodged

NA = Not applied

NP = Not patched (due to reaction achieved)

N9G = No ninth grading

3.2.4 Evaluation of Responses

All responses were graded by a trained dermatologic evaluator meeting TKL's strict certification requirements to standardize the assignment of response grades.

4.0 NATURE OF STUDY MATERIAL

4.1 STUDY MATERIAL SPECIFICATIONS

Identification : Crème, ENG075488, P.S. 1-64.1B
Amount Applied : 0.2 g

4.2 STORAGE, HANDLING, AND DOCUMENTATION OF STUDY MATERIAL

Receipt of the material used in this study was documented in a general logbook, which serves as a permanent record of the receipt, storage, and disposition of all study material received by TKL. On the basis of information provided by the Sponsor, the study material was considered reasonably safe for evaluation on human subjects. A sample of the study material was reserved and will be stored for

a period of 6 months. All study material is kept in a locked product storage room accessible to clinical staff members only. At the conclusion of the clinical study, the remaining study material was discarded or returned to the Sponsor and the disposition documented in the logbook.

4.3 APPLICATION OF STUDY MATERIAL

All study material was supplied by the Sponsor. Material was applied in an amount proportionate to the patch type or as requested by the Sponsor, generally 0.2 mL or g or an amount sufficient to cover the 2 cm x 2 cm patch. The patches were applied to the infrascapular area of the back, either to the right or left of the midline, or to the upper arm. Unless otherwise directed by the Sponsor, the study material was discarded upon completion of the study.

4.4 DESCRIPTION OF PATCH CONDITIONS

Material evaluated under occlusive patch conditions is applied to a 2 cm x 2 cm Webril™ pad attached to a non-porous, plastic film adhesive bandage (3M medical tape). The patch is secured with hypoallergenic tape (Micropore), as needed.

Material evaluated under semi-occlusive patch conditions is applied to a 2 cm x 2 cm Webril™ pad. The pad is affixed to the skin with hypoallergenic tape (Micropore).

5.0 INTERPRETATION

Sensitization is characterized by an acute allergic contact dermatitis. Typical sensitization reactions begin with an immunologic response in the dermis resulting in erythema, edema formation, and secondary epidermal damage (vesiculation), sometimes extending beyond the patch site and often accompanied by itching. Sensitization reactions tend to be delayed. The reaction typically becomes evident between 24 and 48 hours, peaks at 48-72 hours and subsequently subsides. The reaction is often greater at 72 hours than at 48 hours. The severity of the reaction is generally greater during the Challenge Phase of a Repeated Insult Patch Test (RIPT) than that seen during Induction.

Irritant reactions are characterized as a non-immunologic, localized, superficial, exudative, inflammatory response of the skin due to an externally applied material. The typical initial reaction does not develop much edema or vesiculation but results in scaling, drying, cracking, oozing, crusting, and erosions. The reaction is usually sharply delineated, not spreading beyond the patch site. Irritant reactions are typically evident by 24 hours and diminish over the next 48-72 hours. Removal of the offending agent results in gradual improvement of the epidermal damage. The reaction seen at 72 hours is, therefore, less severe than that seen at 48 hours. Finally, the severity of the reaction experienced in the Challenge Phase is generally similar to that seen during Induction.

If the results of the study indicate the likelihood of sensitization, the recommended practice is to rechallenge the subjects who have demonstrated sensitization-like reactions to confirm that these reactions are, indeed, associated with the product. TKL's preferred Rechallenge procedure involves the application of the product to naive sites, under both occlusive and semi-occlusive patch conditions. Use of the semi-occlusive patch condition helps to differentiate irritant and sensitization reactions. Generally speaking, if a product is a sensitizer it will produce a similar reaction under

both occlusion and semi-occlusion. Whereas, if the product has caused an irritant reaction, the reactions will be less pronounced under the semi-occlusive condition.

6.0 DOCUMENTATION AND RETENTION OF DATA

The case report forms (CRFs) were designed to identify each subject by subject number and initials, and to record demographics, examination results, AEs, and end of study status. Originals or copies of all CRFs, correspondence, study reports, and all source data will be kept on hard-copy file for a minimum of 5 years from completion of the study. Storage was maintained either at a TKL facility in a secured room accessible only to TKL employees, or at an offsite location which provided a secure environment with burglar/fire alarm systems, camera detection and controlled temperature and humidity. Documentation will be available for the Sponsor's review on the premises of TKL.

7.0 RESULTS AND DISCUSSION

One hundred twenty (120) subjects between the ages of 18 and 70 were enrolled and 101 completed the study (see Tables 1 and 2 in Appendix I and Data Listings 1 and 2 in Appendix II). The following table summarizes subject enrollment and disposition:

Number enrolled:		120
Number discontinued:		19
Lost to follow-up:	13	
Voluntary withdrawal:	4	
Protocol violation: (114, inadvertently enrolled, history of Lupus)	1	
Other reason: (007: tape reaction)	1	
Number completed:		101

Source: Table 1, Appendix I

There were no adverse events (AEs) reported during the study.

A summary of response data is provided in Table 3, Appendix I. Individual dermatological response grades are provided in Data Listing 3, Appendix II.

8.0 CONCLUSION

Under the conditions employed in this study, there was no evidence of sensitization or significant irritation to product, ENG075488, P.S. 1-64.1B.

9.0 REFERENCES

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APPENDIX I

SUMMARY TABLES

Table 1: Summary of Subject Enrollment and Disposition

	N (%)
Subjects enrolled	120
Subjects completed induction phase	101 (84.2)
Subjects completed all phases	101 (84.2)
Total subjects discontinued	19 (15.8)
Lost to follow-up	13 (10.8)
Voluntary withdrawal	4 (3.3)
Protocol violation	1 (0.8)
Other reasons	1 (0.8)

Note: All percentages are relative to total subjects enrolled.

See data listing 1 for further detail.

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Table 2: Summary of Subject Demographics
All Enrolled Subjects

Age	
N (%) 18 to 44	36 (30.0)
N (%) 45 to 65	71 (59.2)
N (%) 66 and up	13 (10.8)
Mean (SD)	49.5 (13.9)
Median	51.8
Range	18.0 to 70.8
Gender	
N (%) Male	30 (25.0)
N (%) Female	90 (75.0)
Race	
Asian	4 (3.3)
Black	24 (20.0)
Caucasian	73 (60.8)
Hispanic	18 (15.0)
Other	1 (0.8)

See data listing 2 for further detail.

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TKL Study No. DS101515
Table 3: Summary of Dermatologic Response Grades
Number of Subjects by Product

Product = ENG075488, P.S.1-64.1B

	Induction Reading										Challenge Phase		
Response (ESO)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Make Up**	**48hr**	**72hr**	**96hr***
0	107	103	104	98	100	100	99	98	96	6	101	101	
Total evaluable	107	103	104	98	100	100	99	98	96	6	101	101	
Number absent	0	1	0	0	0	0	0	0	5	.	0	0	
Number absent	5	5	2	6	4	4	3	3	0	.	0	0	
Number discontinued	8	11	14	16	16	16	18	19	19	.	19	19	

Maximum Elicited Response During Induction
All Subjects Completing Induction (N=101)

Response	**n(%) Subjects**
0	101 (100.0%)

Total Irritation Score at Induction: 0

See Table 3.1 for key to symbols and scores

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Table 3: Summary of Dermatologic Response Grades
Number of Subjects by Product

Product = SLS 0.1% LOT# 000844251

	Induction Reading										Challenge Phase		
Response	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**Make Up**	**48hr**	**72hr**	**96hr(*)**
-	99	91	83	74	72	74	68	68	70	4	99	99	
?	7	6	12	12	8	11	11	5	5	0	1	2	
+	1	7	9	10	11	5	10	11	7	2	1	0	
+D	0	0	0	2	7	2	0	3	2	0	0	0	
Total evaluable	107	104	104	98	98	92	89	87	84	6	101	101	
Number absent	5	5	2	6	4	4	3	3	3		0	0	
Number discontinued	8	11	14	16	16	16	18	19	19		19	19	
Patch not applied	0	0	0	0	2	8	10	11	14		0	0	

Maximum Elicited Response During Induction
All Subjects Completing Induction (N=101)

Response	**n(%) Subjects**
-	59 (58.4%)
?	10 (9.9%)
+	16 (15.8%)
+D	16 (15.8%)

Total Irritation Score at Induction: 406

(*) when required

See Table 3.1 for Key to Symbols and Scores

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TKL Study No. DS101515

Table 3.1: Key To Symbols and Scores

Score or Symbol	Response or Description of Reaction
	Erythema Results
-	No reaction
?	Minimal or doubtful response, slightly different from surrounding normal skin
+	Definite erythema, no edema
++	Definite erythema, definite edema
+++	Definite erythema, definite edema and vesiculation
	Additional Comments
X	Reading not performed due to missed visit or subject discontinuation
D	Damage to epidermis: oozing, crusting and/or superficial erosions
E	Marked/severe erythema
I	Itching
p	Papular response >50%
pv	Papulovesicular response >50%
S	Spreading of reaction beyond patch site
NP	Not patched due to reaction achieved
PD	Patch dislodged
N9G	No ninth grading
NA	Not applied

TKL Study No. DS101515

Table 3.1: Key To Symbols and Scores

Score or Symbol	Response or Description of Reaction
	Erythema and Elevated Responses (E)
0	No reaction
1	Minimal or doubtful response, slightly different from surrounding normal skin
2	Definite erythema, no edema
3	Definite erythema, definite edema
4	Definite erythema, definite edema and vesiculation
SPECIAL NOTATIONS	
E	Marked/severe erythema
S	Spreading of reaction beyond patch site (ie, reaction where material was not in contact to skin.)
p	Papular response > 50%
pv	Papulovesicular response > 50%
D	Damage to epidermis: oozing, crusting and/or superficial erosions
I	Itching
X	Subjext absent
PD	Patch dislodged
NA	Not applied
NP	Not patched (due to reaction achieved)
N9G	No ninth grading

APPENDIX II

DATA LISTINGS

Data Listing 1: Subject Enrollment and Disposition

	Study Dates						
Subject No.	Screened	1st Applic	Chall Applic	Ended	Last Reading #	Completion Status	Days in Study
001	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
002	03/02/15	03/02/15	--	03/09/15	I1	L	8
003	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
004	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
005	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
006	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
007	03/02/15	03/02/15	--	03/06/15	I2	O	5
008	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
009	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
010	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
011	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
012	03/02/15	03/02/15	--	03/06/15	I0	L	5
013	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
014	03/02/15	03/02/15	--	03/06/15	I0	L	5
015	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
016	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
017	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
018	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
019	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
020	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
021	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
022	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
023	03/02/15	03/02/15	--	03/09/15	I1	L	8
024	03/02/15	03/02/15	04/07/15	04/10/15	C2	C	40
025	03/02/15	03/02/15	--	03/06/15	I0	L	5
026	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
027	03/02/15	03/02/15	04/07/15	04/10/15	C.	C	40
028	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
029	03/06/15	03/06/15	--	03/11/15	I1	S	6
030	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
031	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
032	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
033	03/06/15	03/06/15	--	03/11/15	I0	L	6

Key:
Last Reading # (I=Induction Phase, C=Challenge Phase)
Completion Status (C=Completed, L=Lost to follow-up, S=Voluntary withdrawal, V=Protocol violation, AE=Adverse event, O=Other)

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Data Listing 1: Subject Enrollment and Disposition

	Study Dates						
Subject No.	Screened	1st Applic	Chall Applic	Ended	Last Reading #	Completion Status	Days in Study
034	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
035	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
036	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
037	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
038	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
039	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
040	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
041	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
042	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
043	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
044	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
045	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
046	03/06/15	03/06/15	--	03/18/15	I3	S	13
047	03/06/15	03/06/15	--	03/25/15	I6	L	20
048	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
049	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
050	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
051	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
052	03/06/15	03/06/15	--	03/16/15	I2	S	11
053	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
054	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
055	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
056	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
057	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
058	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
059	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
060	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
061	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
062	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
063	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
064	03/06/15	03/06/15	04/07/15	04/10/15	C2	C	36
065	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
066	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36

Key:
Last Reading # (I=Induction Phase, C=Challenge Phase)
Completion Status (C=Completed, L=Lost to follow-up, S=Voluntary withdrawal, V=Protocol violation, AE=Adverse event, O=Other)

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Data Listing 1: Subject Enrollment and Disposition

	Study Dates						
Subject No.	Screened	1st Applic	Chall Applic	Ended	Last Reading #	Completion Status	Days in Study
067	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
068	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
069	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
070	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
071	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
072	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
073	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
074	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
075	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
076	03/06/15	03/06/15	--	03/11/15	I0	L	6
077	03/06/15	03/06/15	--	03/11/15	I0	L	6
078	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
079	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
080	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
081	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
082	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
083	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
084	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
085	03/06/15	03/06/15	--	03/25/15	I7	S	20
086	03/06/15	03/06/15	--	03/23/15	I6	L	18
087	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
088	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
089	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
090	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
091	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
092	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
093	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
094	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
095	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
096	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
097	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
098	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
099	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36

Key:
Last Reading # (I=Induction Phase, C=Challenge Phase)
Completion Status (C=Completed, L=Lost to follow-up, S=Voluntary withdrawal, V=Protocol violation, AE=Adverse event, O=Other)

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Data Listing 1: Subject Enrollment and Disposition

	Study Dates						
Subject No.	Screened	1st Applic	Chall Applic	Ended	Last Reading #	Completion Status	Days in Study
100	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
101	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
102	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
103	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
104	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
105	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
106	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
107	03/06/15	03/06/15	--	03/11/15	I0	L	6
108	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
109	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
110	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
111	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
112	03/06/15	03/06/15	--	03/16/15	I3	L	11
113	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
114	03/06/15	03/06/15	--	03/11/15	I2	V	6
115	03/06/15	03/06/15	--	03/11/15	I0	L	6
116	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
117	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
118	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
119	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36
120	03/06/15	03/06/15	04/07/15	04/10/15	C.	C	36

Key:
Last Reading # (I=Induction Phase, C=Challenge Phase)
Completion Status (C=Completed, L=Lost to follow-up, S=Voluntary withdrawal, V=Protocol violation, AE=Adverse event, O=Other)

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Data Listing 2: Subject Demographics

Subject No.	Age	Gender	Race
001	29.9	Male	Caucasian
002	46.1	Female	Hispanic
003	69.4	Female	Caucasian
004	64.5	Male	Caucasian
005	58.9	Female	Caucasian
006	55.0	Female	Caucasian
007	54.5	Female	Asian
008	62.7	Female	Caucasian
009	42.2	Female	Black
010	43.5	Male	Black
011	61.2	Female	Caucasian
012	47.4	Female	Hispanic
013	62.6	Female	Caucasian
014	25.6	Female	Hispanic
015	65.2	Female	Caucasian
016	50.6	Female	Hispanic
017	54.0	Female	Caucasian
018	50.1	Female	Hispanic
019	18.0	Female	Hispanic
020	53.6	Female	Black
021	18.6	Male	Caucasian
022	39.7	Male	Black
023	35.6	Female	Hispanic
024	48.5	Female	Caucasian
025	22.5	Female	Caucasian
026	28.4	Female	Caucasian
027	47.0	Male	Black
028	49.2	Female	Caucasian
029	48.5	Female	Caucasian
030	67.0	Female	Caucasian
031	50.7	Female	Black
032	66.4	Female	Black
033	49.5	Female	Black
034	55.3	Female	Hispanic
035	62.2	Female	Caucasian
036	61.2	Female	Caucasian
037	64.5	Female	Caucasian

Data Listing 2: Subject Demographics

Subject No.	Age	Gender	Race
038	60.9	Female	Black
039	50.4	Female	Caucasian
040	66.5	Male	Caucasian
041	68.6	Male	Caucasian
042	66.6	Female	Asian
043	53.9	Female	Caucasian
044	53.2	Female	Caucasian
045	69.5	Female	Caucasian
046	55.4	Female	Black
047	34.3	Male	Hispanic
048	36.7	Female	Black
049	52.0	Female	Caucasian
050	31.9	Male	Caucasian
051	67.3	Female	Caucasian
052	38.4	Female	BI-RACIAL
053	58.1	Female	Caucasian
054	58.7	Male	Caucasian
055	64.8	Female	Black
056	43.3	Female	Caucasian
057	56.9	Female	Caucasian
058	53.8	Female	Caucasian
059	51.5	Male	Caucasian
060	68.1	Female	Caucasian
061	45.6	Female	Black
062	54.4	Male	Caucasian
063	22.7	Female	Caucasian
064	64.6	Female	Caucasian
065	39.9	Female	Black
066	51.0	Male	Caucasian
067	60.7	Female	Hispanic
068	33.7	Female	Caucasian
069	66.5	Female	Caucasian
070	70.8	Female	Caucasian
071	63.3	Female	Caucasian
072	46.9	Female	Caucasian
073	49.6	Male	Caucasian
074	52.0	Female	Hispanic

Data Listing 2: Subject Demographics

Subject No.	Age	Gender	Race
075	18.9	Female	Caucasian
076	31.6	Female	Caucasian
077	19.2	Male	Caucasian
078	48.2	Female	Caucasian
079	44.8	Male	Caucasian
080	67.9	Female	Caucasian
081	42.9	Female	Black
082	20.4	Male	Black
083	49.0	Female	Caucasian
084	58.8	Female	Hispanic
085	24.6	Female	Black
086	51.1	Male	Caucasian
087	42.2	Male	Caucasian
088	55.7	Male	Caucasian
089	56.2	Female	Caucasian
090	28.4	Male	Black
091	31.3	Female	Hispanic
092	60.3	Female	Caucasian
093	50.5	Female	Asian
094	56.0	Female	Caucasian
095	54.0	Female	Caucasian
096	33.6	Female	Hispanic
097	57.2	Male	Caucasian
098	42.7	Female	Caucasian
099	47.2	Male	Hispanic
100	55.9	Female	Black
101	48.9	Female	Asian
102	60.4	Male	Caucasian
103	55.5	Female	Black
104	54.8	Female	Caucasian
105	57.0	Female	Caucasian
106	60.3	Female	Caucasian
107	22.5	Female	Black
108	70.7	Male	Caucasian
109	55.4	Female	Black
110	63.5	Female	Black
111	65.8	Female	Caucasian
112	54.3	Female	Caucasian
113	48.5	Female	Caucasian
114	28.7	Female	Caucasian
115	55.5	Male	Black
116	31.9	Male	Caucasian
117	18.1	Female	Caucasian
118	30.7	Male	Hispanic
119	49.5	Male	Hispanic
120	41.5	Female	Hispanic

[redacted]

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
001	0	0	0	0	0	0	0	0	0		0	0	0	
002	0	X	X	X	X	X	X	X	X		0	X	X	
003	0	0	0	0	0	0	0	0	0		0	0	0	
004	0	0	0	0	0	0	0	0	0		0	0	0	
005	0	0	0	0	0	0	0	X	0	0	0	0	0	
006	0	0	0	0	0	0	0	0	0		0	0	0	
007	0	0	X	X	X	X	X	X	X		0	X	X	
008	0	0	0	0	0	0	0	X	0	0	0	0	0	
009	0	0	0	0	0	0	0	0	0		0	0	0	
010	0	0	0	0	0	0	0	0	0		0	0	0	
011	0	0	0	0	0	0	0	0	0		0	0	0	
012	X	X	X	X	X	X	X	X	X		.	X	X	
013	X	0	0	0	0	0	0	0	0	0	0	0	0	
014	X	X	X	X	X	X	X	X	X		.	X	X	
015	0	0	0	0	0	0	0	0	0		0	0	0	
016	0	0	0	0	0	0	0	0	0		0	0	0	
017	0	0	0	0	0	0	0	0	0		0	0	0	
018	0	0	0	0	0	0	0	0	0		0	0	0	
019	0	0	0	0	0	0	0	0	0		0	0	0	
020	0	0	0	0	0	0	0	0	0		0	0	0	
021	0	0	0	X	0	0	0	0	0	0	0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

[redacted]

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
022	0	0	0	0	0	0	0	0	0		0	0	0	
023	0	X	X	X	X	X	X	X	X		0	X	X	
024	0	0	0	0	X	0	0	0	0	0	0	0	0	
025	X	X	X	X	X	X	X	X	X		.	X	X	
026	0	0	0	X	0	0	0	0	0	0	0	0	0	
027	0	0	0	0	0	0	0	0	0		0	0	0	
028	0	0	0	0	0	0	0	0	0		0	0	0	
029	0	X	X	X	X	X	X	X	X		0	X	X	
030	0	0	0	0	0	0	0	0	0		0	0	0	
031	0	0	0	0	0	0	0	0	0		0	0	0	
032	0	0	0	0	0	0	0	0	0		0	0	0	
033	X	X	X	X	X	X	X	X	X		.	X	X	
034	0	0	0	0	0	0	0	X	0	N9G	0	0	0	
035	0	0	0	0	0	0	0	0	0		0	0	0	
036	0	0	0	0	0	0	0	0	0		0	0	0	
037	0	0	0	0	0	0	0	0	0		0	0	0	
038	0	0	0	0	0	0	0	0	0		0	0	0	
039	0	0	0	0	0	0	0	0	0		0	0	0	
040	0	0	0	0	0	0	0	0	0		0	0	0	
041	0	0	0	0	0	0	0	0	0		0	0	0	
042	0	X	0	0	0	0	0	0	0	N9G	0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
043	0	0	0	0	0	0	0	0	0		0	0	0	
044	0	0	0	0	0	0	0	0	0		0	0	0	
045	0	0	0	0	0	0	0	0	0		0	0	0	
046	0	0	0	X	X	X	X	X	X		0	X	X	
047	0	0	0	0	0	0	X	X	X		0	X	X	
048	X		0	0	0	0	0	0	0	N9G	0	0	0	
049	0	0	0	0	0	0	0	0	0		0	0	0	
050	0	0	0	0	0	0	0	0	0		0	0	0	
051	0	0	0	0	0	0	0	0	0		0	0	0	
052	0	0	X	X	X	X	X	X	X		0	X	X	
053	0	0	0	0	0	0	0	0	0		0	0	0	
054	0	0	0	0	0	0	0	0	0		0	0	0	
055	0	0	0	0	0	0	0	0	0		0	0	0	
056	X	0	0	0	0	0	0	0	0	N9G	0	0	0	
057	0	0	0	0	0	0	0	0	0		0	0	0	
058	0	0	0	0	0	0	0	0	0		0	0	0	
059	0	0	0	0	0	0	0	0	0		0	0	0	
060	0	0	0	0	0	0	0	0	0		0	0	0	
061	0	0	0	X	0	0	0	0	0	N9G	0	0	0	
062	0	0	0	X	0	0	0	0	0	N9G	0	0	0	
063	0	0	0	0	0	0	0	0	0		0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
064	0	0	0	0	0	0	0	0	0		0	0	0	
065	0	0	0	0	0	0	0	0	N9G		0	0	0	
066	0	0	0	0	X	0	0	0	0	N9G	0	0	0	
067	0	0	0	0	0	0	0	0	0		0	0	0	
068	0	0	0	0	0	X	0	0	0	N9G	0	0	0	
069	0	0	0	0	0	0	0	0	0		0	0	0	
070	0	0	0	0	0	0	0	0	N9G		0	0	0	
071	0	0	0	0	0	0	0	0	0		0	0	0	
072	0	0	0	0	0	0	0	0	0		0	0	0	
073	0	0	0	0	0	0	X	0	0	N9G	0	0	0	
074	0	0	0	0	0	0	0	0	0		0	0	0	
075	0	0	0	0	0	0	0	0	N9G		0	0	0	
076	X	X	X	X	X	X	X	X	X		.	X	X	
077	X	X	X	X	X	X	X	X	X		.	X	X	
078	0	0	0	0	0	0	0	0	0		0	0	0	
079	0	0	X	0	0	0	0	0	0	N9G	0	0	0	
080	0	0	0	0	0	0	0	0	0		0	0	0	
081	0	0	0	0	0	0	0	0	0		0	0	0	
082	0	0	0	X	0	0	0	0	0	N9G	0	0	0	
083	0	0	0	0	0	0	0	0	0		0	0	0	
084	0	0	0	0	0	0	0	0	0		0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

[redacted]

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
085	0	0	0	0	X	0	0	X	X		0	X	X	
086	0	0	X	0	0	0	X	X	X		0	X	X	
087	0	0	0	0	0	0	0	0	0		0	0	0	
088	0	0	0	0	0	0	0	0	0		0	0	0	
089	0	0	0	0	0	0	X	0	0	N9G	0	0	0	
090	X	0	0	0	0	0	0	0	0	N9G	0	0	0	
091	0	0	0	0	0	0	0	0	0		0	0	0	
092	0	0	0	0	0	0	0	0	0		0	0	0	
093	0	0	0	0	0	0	0	0	0		0	0	0	
094	0	0	0	0	0	0	0	0	0		0	0	0	
095	0	0	0	0	0	0	0	0	N9G		0	0	0	
096	0	X	0	0	0	0	0	0	0	N9G	0	0	0	
097	0	0	0	0	0	0	0	0	0		0	0	0	
098	0	0	0	0	0	X	0	0	0	N9G	0	0	0	
099	0	X	0	0	0	0	0	0	0	N9G	0	0	0	
100	0	X	0	0	0	0	0	0	0	N9G	0	0	0	
101	0	0	0	0	0	0	0	0	0		0	0	0	
102	0	0	0	0	0	0	0	0	0		0	0	0	
103	0	0	0	0	0	0	0	0	0		0	0	0	
104	0	0	0	0	0	0	0	0	0		0	0	0	
105	0	0	0	0	0	0	0	0	0		0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

[redacted]

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = ENG075488, P.S.1-64.1B

	Induction Reading											Challenge Phase		
Subject No.	1 ESO	2 ESO	3 ESO	4 ESO	5 ESO	6 ESO	7 ESO	8 ESO	9 ESO	MU	Total Score	48hr	72hr	96hr(*)
106	0	0	0	0	0	X	0	0	0	N9G	0	0	0	
107	X	X	X	X	X	X	X	X	X		.	X	X	
108	0	0	0	0	0	0	0	0	0		0	0	0	
109	0	0	0	0	0	X	0	0	0	N9G	0	0	0	
110	0	0	0	0	0	0	X	0	0	N9G	0	0	0	
111	0	0	0	0	0	0	0	0	0		0	0	0	
112	X	0	0	X	X	X	X	X	X		0	X	X	
113	0	0	0	0	0	0	0	0	0		0	0	0	
114	0	0	X	X	X	X	X	X	X		0	X	X	
115	X	X	X	X	X	X	X	X	X		.	X	X	
116	0	0	0	X	0	0	0	0	0	N9G	0	0	0	
117	0	0	0	0	0	0	0	0	N9G		0	0	0	
118	0	0	0	0	0	0	0	0	0		0	0	0	
119	0	X	0	0	0	0	0	0	0	N9G	0	0	0	
120	0	0	0	0	X	0	0	0	0	N9G	0	0	0	

(*) when required
E = Induction Grade S = Superficial Grade O = Other response MU = Make-up visit
See Table 3.1 for Key to Symbols and Scores
Generated on 04/15/15:11:43 by DETAIL8N.SAS/USES: NTRESPONSE, PRODLIST

TKL RESEARCH
TKL Study No. DS101515

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = SLS 0.1% LOT# 000844251

Subject No.	Induction Reading										Challenge Phase		
	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
001	-	-	-	+	+D	NP	NP	NP	NP		-	-	
002	-	X	X	X	X	X	X	X	X		X	X	
003	-	-	-	-	-	-	-	-	-		-	-	
004	-	-	-	-	-	-	-	-	-		-	-	
005	-	-	-	-	-	-	-	X	-	-	-	-	
006	-	-	-	-	-	-	-	-	-		-	-	
007	-	-	X	X	X	X	X	X	X		X	X	
008	-	-	-	-	-	-	?	X	-	-	-	-	
009	-	-	-	-	-	-	-	-	-		-	-	
010	-	-	-	-	-	-	-	-	-		-	-	
011	-	-	-	-	-	-	-	-	-		-	-	
012	X	X	X	X	X	X	X	X	X		X	X	
013	X	-	-	-	-	-	-	-	-	-	-	-	
014	X	X	X	X	X	X	X	X	X		X	X	
015	-	-	-	-	-	-	-	-	-		-	-	
016	-	-	-	-	-	-	-	-	-		-	-	
017	-	-	-	-	?	?	?	-	-		-	-	
018	-	-	-	-	-	?	+	?	-		-	-	
019	-	-	-	-	-	-	-	-	-		-	-	
020	-	-	-	-	-	-	-	-	-		-	-	
021	-	-	?	X	-	-	+	?	?	+	-	-	
022	-	-	-	-	-	-	-	-	-		-	-	
023	-	X	X	X	X	X	X	X	X		X	X	

See Table 3.1 for Key to Symbols and Scores

MU = Make-up reading for missed induction visit

(*) When required
Generated on 04/15/15: 9:13 by DETAIL.SAS/USES: RESPONSE, PRODLIST

TKL RESEARCH
TKL Study No. DS101515

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = SLS 0.1% LOT# 000844251

	Induction Reading										Challenge Phase		
Subject No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
024	-	-	-	-	X	-	-	-	-	+	-	-	
025	X	X	X	X	X	X	X	X	X		X	X	
026	-	-	-	X	-	-	-	-	-	-	-	-	
027	-	-	-	-	-	-	-	-	-		-	-	
028	-	-	-	-	?	?	?	+	+		-	-	
029	-	X	X	X	X	X	X	X	X		X	X	
030	-	-	-	-	-	-	-	-	-		-	-	
031	-	-	-	-	-	-	+	+D	NP		-	-	
032	-	-	-	-	?	?	-	-	-		-	-	
033	X	X	X	X	X	X	X	X	X		X	X	
034	?	+	+	+	+	+	+	X	?	N9G	-	-	
035	-	-	-	-	-	-	-	-	-		-	-	
036	-	-	-	-	?	-	-	-	-		-	-	
037	-	-	-	-	-	-	-	-	-		-	-	
038	-	-	-	-	-	-	-	-	-		-	-	
039	-	-	-	-	-	-	-	-	-		-	-	
040	-	-	?	?	+	?	-	-	-		-	-	
041	?	?	?	-	?	?	-	-	-		-	-	
042	-	X	-	-	-	-	-	-	-	N9G	-	-	
043	-	-	-	-	-	-	?	+	+		-	-	
044	-	-	-	?	-	-	-	-	-		-	-	
045	-	-	-	-	-	-	-	-	-		-	-	
046	-	-	-	X	X	X	X	X	X		X	X	

(*) When required
Generated on 04/15/15: 9:13 by DETAIL.SAS/USES: RESPONSE, PRODLIST

TKL RESEARCH
TKL Study No. DS101515

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = SLS 0.1% LOT# 000844251

Subject No.	Induction Reading										Challenge Phase		
	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
047	-	-	-	-	-	-	X	X	X		X	X	
048	X	-	-	-	-	-	-	-	-	N9G	-	-	
049	-	-	-	-	-	-	-	-	-		-	-	
050	-	-	?	+	+D	NP	NP	NP	NP		-	-	
051	?	-	-	+	+	+D	NP	NP	NP		-	-	
052	-	-	X	X	X	X	X	X	X		X	X	
053	-	-	-	-	-	-	-	-	-		-	-	
054	-	-	-	?	+	+	+	+D	NP		-	-	
055	-	-	-	-	-	-	-	-	-		-	-	
056	X	-	-	-	-	-	-	-	-	N9G	-	-	
057	-	-	-	-	-	-	-	-	-		-	-	
058	-	-	-	-	?	-	?	+	?		-	-	
059	-	-	-	-	-	-	-	-	-		-	-	
060	-	-	-	-	?	?	?	+	+		-	-	
061	-	-	-	X	-	-	-	-	-	N9G	-	-	
062	-	-	-	X	-	-	-	-	-	N9G	-	-	
063	-	-	-	?	+	?	?	+	+D		-	-	
064	?	?	+	+	+D	NP	NP	NP	NP		-	-	
065	-	-	-	-	-	-	?	+	N9G		-	-	
066	-	-	-	-	X	-	-	-	-	N9G	-	-	
067	?	?	?	?	+	?	?	+	+		-	-	
068	-	+	+	?	+	X	-	?	?	N9G	-	-	
069	-	-	-	-	-	-	-	?	?		-	-	

(*) When required
Generated on 04/15/15: 9:13 by DETAIL.SAS/USES: RESPONSE, PRODLIST

TKL RESEARCH
TKL Study No. DS101515

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = SLS 0.1% LOT# 000844251

Subject No.	Induction Reading										Challenge Phase		
	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
070	-	-	-	?	-	-	-	-	N9G		-	-	
071	-	-	-	-	-	-	-	-	-		-	-	
072	-	?	?	?	+	+	+	+	+		-	-	
073	-	-	-	-	-	-	X	-	-	N9G	-	-	
074	-	-	-	-	-	-	-	-	-		-	-	
075	-	-	?	?	+	?	+	+	N9G		-	-	
076	X	X	X	X	X	X	X	X	X		X	X	
077	X	X	X	X	X	X	X	X	X		X	X	
078	-	+	+	+	?	+	+	?	+		-	-	
079	-	-	X	-	-	-	-	-	-	N9G	-	-	
080	-	-	-	-	-	-	-	-	-		-	-	
081	-	-	-	-	-	-	-	-	-		-	-	
082	-	-	-	X	-	-	-	-	-	N9G	-	-	
083	?	?	?	?	+	+	+	+	+D		-	-	
084	-	-	-	-	-	-	-	-	-		-	-	
085	-	-	-	-	X	-	-	X	X		X	X	
086	-	-	X	-	-	?	X	X	X		X	X	
087	-	-	?	?	-	-	-	-	-		-	-	
088	-	?	?	-	-	-	?	+	+		-	-	
089	-	+	+	+	+D	NP	X	NP	NP	NP	-	-	
090	X	-	-	-	-	-	-	-	-	N9G	-	-	
091	-	-	-	-	-	-	-	-	-		-	-	
092	-	-	?	?	+	+D	NP	NP	NP		-	-	

(*) When required
Generated on 04/15/15: 9:13 by DETAIL.SAS/USES: RESPONSE, PRODLIST

TKL RESEARCH
TKL Study No. DS101515

Data Listing 3: Dermatologic Response Grades
By Product and Subject

Product = SLS 0.1% LOT# 000844251

	Induction Reading										Challenge Phase		
Subject No.	1	2	3	4	5	6	7	8	9	MU	48hr	72hr	96hr(*)
093	-	-	-	-	-	-	?	-	-		-	-	
094	-	-	-	-	-	-	-	-	-		-	-	
095	-	-	?	+	+D	NP	NP	NP	NP		-	-	
096	-	X	-	-	-	-	-	-	-	N9G	-	-	
097	-	-	+	+D	NP	NP	NP	NP	NP		?	?	
098	-	-	-	-	-	X	-	-	-	N9G	-	-	
099	-	X	-	-	-	-	-	-	-	N9G	-	-	
100	-	X	-	-	-	-	-	-	-	N9G	-	-	
101	+	+	+	+	+D	NP	NP	NP	NP		+	?	
102	-	-	-	-	-	-	+	+D	NP		-	-	
103	-	-	-	-	-	-	-	-	-		-	-	
104	-	-	-	-	-	-	-	-	-		-	-	
105	-	-	-	-	-	-	-	-	-		-	-	
106	?	+	+	+D	NP	X	NP	NP	NP	NP	-	-	
107	X	X	X	X	X	X	X	X	X		X	X	
108	-	-	-	-	-	-	-	-	-		-	-	
109	-	-	-	-	-	X	-	-	-	N9G	-	-	
110	-	-	-	-	-	-	X	-	-	N9G	-	-	
111	-	-	-	-	-	-	-	-	-		-	-	
112	X	-	-	X	X	X	X	X	X		X	X	
113	-	-	-	-	-	-	-	-	-		-	-	
114	-	-	X	X	X	X	X	X	X		X	X	
115	X	X	X	X	X	X	X	X	X		X	X	
116	-	-	-	X	-	-	-	-	-	N9G	-	-	
117	-	+	+	+	+D	NP	NP	NP	NP		-	-	
118	-	-	-	-	-	-	-	-	-		-	-	
119	-	X	-	-	-	-	-	-	-	N9G	-	-	
120	-	-	-	-	X	-	-	-	-	N9G	-	-	

(*) When required
Generated on 04/15/15: 9:13 by DETAIL.SAS/USES: RESPONSE, PRODLIST

Consumer Product Testing Co.

ESTABLISHED 1975

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

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

TEST MATERIAL: Face Mask - ENG079835-0.11, PS16-48.1

contains 0.005% Hordeum Vulgare Extract

EXPERIMENT REFERENCE NUMBER: C16-0735.01

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

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

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

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

Consumer Product Testing Co.

EST. 1975

QUALITY ASSURANCE UNIT STATEMENT

Study Number: C16-0735.01

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.

Charles Sisto
Quality Assurance Representative

04-13-2016
Date

70 New Dutch Lane • Fairfield, New Jersey 07004-2514 • (973) 808-7111 • Fax (973) 808-7234
Clinical • Toxicology • Analytical Chemistry • Microbiology

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 sixteen (116) qualified subjects, male and female, ranging in age from 18 to 79 years, were selected for this evaluation. One hundred ten (110) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

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

Exclusion Criteria:

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

Test Material: Face Mask - ENG079835-0.11, PS16-48.1

Study Schedule:

Panel #	Initiation Date	Completion Date
20160046	February 22, 2016	March 31, 2016
20160048	February 24, 2016	March 31, 2016

[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 one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

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

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

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

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

Adverse Events:

On March 13, 2016, Subject #17, Panel 20160046, was hospitalized with chest pain, which was considered a serious adverse event. She was discharged on March 14, 2016, with a diagnosis of unstable angina pectoris. It was the Principal Investigator's opinion that this occurrence was unlikely related to the test material.

Amendments:

There were no amendments.

Deviations:

There were no deviations.

Results:

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

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, Face Mask - ENG079835-0.11, PS16-48.1, indicated no potential for dermal irritation or allergic contact sensitization.

[redacted]
C16-0735.01

Table 1
Panel #20160046

Individual Results

Face Mask - ENG079835-0.11, PS16-48.1

Subject Number	Induction Phase									Virgin Challenge Site	
	Day1*	1	2	3	4	5	6	7	8	9	Day 1*	Day 3
1	0	0	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0	0	0
3	----------DID NOT COMPLETE STUDY----------											
4	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	---DNC---	
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

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

Table 1
(continued)
Panel #20160046

Individual Results

Face Mask - ENG079835-0.11, PS16-48.1

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	----------DID NOT COMPLETE STUDY----------											
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	0	0	0	0	0	0	0	0	0	0	0	0
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	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
58	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)
Panel #20160048

Individual Results

Face Mask - ENG079835-0.11, PS16-48.1

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

Day 1* = Supervised removal

Table 1
(continued)
Panel #20160048

Individual Results

Face Mask - ENG079835-0.11, PS16-48.1

Subject Number	Induction Phase									Virgin Challenge Site	
	Day1*	1	2	3	4	5	6	7	8	9	Day 1*	Day 3
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0	0	0	0
51	----------DID NOT COMPLETE STUDY----------											
52	0	0	0	0	0	0	0	0	0	0	0	0
53	0	0	0	0	0	0	0	0	0	0	0	0
54	0	0	0	0	0	0	0	0	0	0	0	0
55	0	0	0	0	0	0	0	0	0	0	0	0
56	0	0	0	0	0	0	0	0	0	0	0	0
57	0	0	0	0	0	0	0	0	0	0	0	0
58	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 2
Panel #20160046

Subject Demographics

Subject Number	Initials	Age	Gender
1	KAM	58	F
2	JCJ	39	F
3	AJD	18	M
4	F-M	73	F
5	DLC	68	M
6	LAN	48	F
7	REF	79	M
8	BAD	72	F
9	RBW	71	F
10	PAS	64	F
11	MPM	66	M
12	DRR	21	M
13	RER	72	F
14	BMA	61	F
15	AJG	49	M
16	A-D	68	F
17	SAF	67	F
18	S-G	72	F
19	JEF	78	F
20	NVR	66	M
21	MPC	79	F
22	K-W	42	F
23	M-P	72	F
24	JCR	75	F
25	J-V	49	F
26	OJS	29	M
27	GLS	58	F
28	NPM	53	M
29	KMC	50	F

Table 2
(continued)
Panel #20160046

Subject Demographics

Subject Number	Initials	Age	Gender
30	AMJ	22	F
31	R-C	78	F
32	K-M	62	F
33	MRB	57	F
34	F-G	70	M
35	EVA	66	F
36	BJR	72	M
37	M-A	68	F
38	RLB	52	M
39	JBR	72	M
40	S-C	47	F
41	H-S	73	F
42	MAN	57	F
43	S-T	50	F
44	DLM	62	F
45	JAN	42	F
46	LAK	51	F
47	L-B	51	F
48	AGS	18	M
49	M-B	45	F
50	SYA	52	F
51	J-B	54	M
52	BIH	71	F
53	M-C	53	F
54	G-B	48	M
55	BBB	74	F
56	BPJ	24	F
57	TLV	54	F
58	J-S	50	F

Table 2
(continued)
Panel #20160048

Subject Demographics

Subject Number	Initials	Age	Gender
1	JCD	57	M
2	MAC	57	M
3	AJD	18	M
4	GCL	65	F
5	AJG	67	M
6	JRN	52	M
7	I-F	50	F
8	DMR	46	F
9	LFD	67	F
10	VLW	49	F
11	L-T	55	M
12	JVS	21	F
13	KMB	30	F
14	EBV	68	F
15	KEB	55	M
16	YMD	32	F
17	KLR	60	F
18	WIS	48	F
19	M-M	31	F
20	K-K	59	F
21	QSK	21	F
22	ASW	19	F
23	TTR	21	M
24	JAC	20	M
25	C-D	33	F
26	ELJ	62	F
27	CMF	65	F
28	RMD	52	M
29	TRM	58	M

Table 2
(continued)
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Subject Demographics

Subject Number	Initials	Age	Gender
30	KSV	25	F
31	LDD	37	F
32	ADC	42	M
33	CLF	48	F
34	LSW	42	F
35	STC	44	F
36	JLL	59	F
37	TLD	44	F
38	RAD	48	M
39	HTW	19	F
40	JMB	39	F
41	RAL	42	F
42	CAR	56	F
43	K-B	62	F
44	J-J	27	M
45	MTM	29	F
46	LEH	70	M
47	E-G	66	F
48	H-R	60	M
49	EMC	65	F
50	CCC	66	M
51	SLR	22	F
52	D-D	55	M
53	NLT	69	F
54	J-B	48	F
55	LER	57	F
56	L-K	63	F
57	TAF	67	F
58	EBF	44	F