
Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

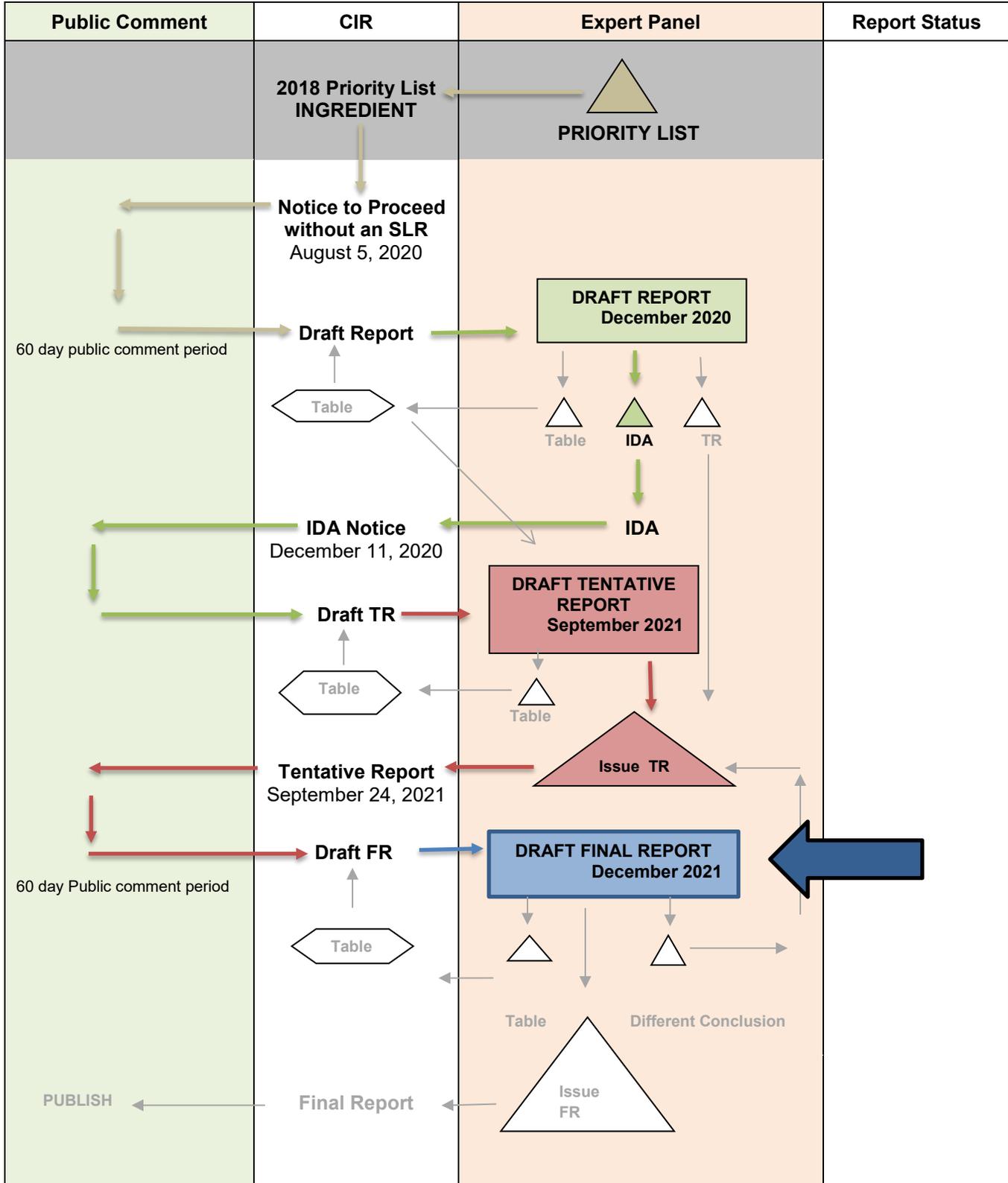
Status: Draft Final Report for Panel Review
Release Date: November 10, 2021
Panel Meeting Date: December 6-7, 2021

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

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Barley-derived Ingredients

MEETING December 2021





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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: November 10, 2021
Subject: Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Final Report of the Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics. (It is identified as *report_Barley_122021* in the pdf document.) At the September 2021 meeting, the Panel issued a Tentative Report with the conclusion that the 4 barley seed-derived ingredients are safe in cosmetics in the present practices of use and concentration described in the safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination that the remaining 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations. The additional data needed to determine safety of these ingredients as used in cosmetics 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 use as a food for ingredients derived from the flower, leaf, stem, and root.

Since the issuance of the Tentative Report, CIR has received no new unpublished data. Updated information regarding gluten content in cosmetics and use of barley grass as a developing functional food have been added to the report. These data are highlighted to aid in the Panel's review. The attached Council comments on the Tentative Report have been addressed (*PCPCcomments_Barley_122021*), as noted in the check sheet immediately following the comments (*response-PCPCcomments_Barley_122021*). In response to a Council comment on gluten and the addition of supporting references, CIR staff noted the quote from a celiac disease researcher that stated "if you have celiac disease, then the application of gluten-containing products to the skin should not be a problem, unless you have skin lesions that allow gluten to be absorbed systemically in great quantities." There are no references cited to support this claim. Should this information be added to the report, and if so, should the damaged skin caveat be added to this report's conclusion?

Additional supporting documents for this report package include a flow chart (*flow_Barley_122021*), report history (*history_Barley_122021*), transcripts (*transcripts_Barley_122021*), search strategy (*search_Barley_122021*), data profile (*datapofile_Barley_122021*), and 2021 VCRP data (*VCRP_Barley_122021*).

The Panel should review the Abstract, Discussion, and Conclusion, and issue a Final Report.



Memorandum

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

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

DATE: October 7, 2021

SUBJECT: Tentative Report: Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics (report released September 24, 2021)

The Personal Care Products Council respectfully submits the following comments on the tentative report, Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics.

Key Issues

The report should indicate that barley sprouts are used as food, for example, see <https://extension.psu.edu/sprouting-the-truth-about-sprouted-grains> . Barley grass (also called barley leaves) is also used as food, for example, see <https://www.healthline.com/nutrition/barley-grass> and [Zeng et al. \(2018\)](#). This information should be added to the non-cosmetic use section.

If the term “malt” is going to be left in the report, it should be defined.

Additional Considerations

Abstract – The abstract should indicate that the four ingredients that are considered safe are derived from seeds.

Introduction – Perhaps a reference more recent than the 1980 CIR report on wheat gluten, such as the 2015 article by the GI Society at <https://badgut.org/information-centre/a-z-digestive-topics/celiac-disease-skin-care-products/> would be a helpful addition to the discussion on gluten in cosmetics.

Dermal Irritation and Sensitization Studies – It would be helpful to add the number of subjects used in each study to the text.

Table 4 – It should be made clear that the “Juice” was a juice of barley grass.

Barley-Derived Ingredients - December 2021 – Christina Burnett	
Comment Submitter: Personal Care Products Council	
Date of Submission: 10/7/2021	
Comment	Response/Action
The report should indicate that barley sprouts are used as food, for example, see https://extension.psu.edu/sprouting-the-truth-about-sprouted-grains . Barley grass (also called barley leaves) is also used as food, for example, see https://www.healthline.com/nutrition/barley-grass and Zeng et al. (2018). This information should be added to the non-cosmetic use section.	Added the Zeng reference but not the Healthline article as CIR does not use non-vetted references (i.e., news articles). The PSU article also appears to be a news article and only generally mentions that barley may be a sprouted grain, but doesn't go into details about common food use.
If the term “malt” is going to be left in the report, it should be defined.	Reworked the first sentence where “malt” appears so that it does not read like malt is an ingredient. Does the Panel still want to include malt in this manner?
Abstract – The abstract should indicate that the four ingredients that are considered safe are derived from seeds.	Added “seed derived-” to the sentence “The Panel concluded that 4 barley...”
Introduction – Perhaps a reference more recent than the 1980 CIR report on wheat gluten, such as the 2015 article by the GI Society at https://badgut.org/information-centre/a-z-digestive-topics/celiac-disease-skin-care-products/ would be a helpful addition to the discussion on gluten in cosmetics.	Added this reference and a reference by Thompson, but changed the wording in the Introduction to reflect the current findings on gluten in cosmetics. Is the new wording acceptable to the Panel? The new reference has a quote that Panel should review regarding damaged skin (see Memo). Should the conclusion have a damaged skin caveat? Also added reference to the Panel’s assessment of hydrolyzed wheat gluten
Dermal Irritation and Sensitization Studies – It would be helpful to add the number of subjects used in each study to the text.	Suggestion accepted.
Table 4 – It should be made clear that the “Juice” was a juice of barley grass.	Suggestion accepted.

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.

September 2021 - The Panel issued a Tentative Report with the conclusion that the following 4 barley-derived ingredients are safe in cosmetics in the present practices of use and concentrations described in this safety assessment:

Hordeum Distichon (Barley) Seed Flour
Hordeum Vulgare Seed Extract

Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water

The Panel noted that the barley seed-derived ingredients that are reviewed in this safety assessment are found in 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 the absorption of these ingredients through the skin is much less than the potential for systemic exposure from absorption through oral exposures. This fact, coupled with negative findings in human dermal irritation and sensitization studies on whole plant extracts and seed extracts, led the Panel to determine that barley seed-derived ingredients are safe for use in cosmetic products.

However, the Panel also concluded that the available data are insufficient to make a determination of safety on the following 12 barley-derived ingredients:

Hordeum Distichon (Barley) Extract
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 Sprout Extract
Hordeum Vulgare Stem Water

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
 - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root.

Barley-Derived Ingredients Data Profile* - December 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

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/opthpv/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.

Full Team Meeting – December 8, 2020

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.

SEPTEMBER 2021 PANEL MEETING – 2ND REVIEW/DRAFT TENTATIVE REPORT

Belsito's Team Meeting – September 13, 2021

DR. BELSITO: Okay, so barley. At the December 2020 meeting, we issued an IDA for the 16 ingredients. In order to come up with a conclusion, we requested a 28-day dermal tox on the whole plant extracts. Both the distichon and the vulgare extract. And, if positive, developments on reprotox and genotox may be needed. Alternatively, if we could determine that they were GRAS for ingredients derived from flower, leaf, stem, and root, those concerns would go away. We requested irritation and sensitization at maximum concentration of use for the whole plant extracts, again both the distichon and the Hordeum Vulgare extract.

We got unpublished human dermal irritation and ocular in-use study and HRIPT in a mascara containing 0.3 percent distichon extract. Of note, it's used up to 1.8. Then HRIPT on a cosmetic -- oh, I'm sorry. HRIPT on a cosmetic product up to 2.76 of the distichon, which covers maximum concentration of use. But 0.005 percent on the vulgare extract, and it's used up to 1.5 percent. I'm not really sure whether that's important, whether these two different strains of *Hordeum* are sufficiently different that we can't use one versus the other.

The use table has been updated. There are leave-on uses. We now have some use for the seed flower, two total uses. One with being generically described as barley flower. So that's what we got, and so, let's look at the text. One question here, just for clarification, on page 22 of the PDF, the second full paragraph on *Hordeum Vulgare* as a 6-rowed barley. The next to the last line, it says, and an intermedium from where the lateral kernels, is that correct, intermedium, or should it be intermediate? Intermedium group, I've never heard of that. It's not critical, but --

MS. BURNETT: I'll go back and check. I'm not sure.

DR. BELSITO: Okay. And, then, of course we'll need the botanical boilerplate, but I guess we dealt with the aflatoxins in the discussion, correct? We said that we wouldn't expect them to be present?

MS. BURNETT: I'm sorry, repeat that again?

DR. BELSITO: This is page --

DR. LIEBLER: Yes, it's on page 28 of the discussion.

DR. BELSITO: Yeah. Yeah. And we have the inhalation boilerplate. So we're still not sure whether leaf, stem, root, and sprouts are GRAS. Is that correct, Christina?

MS. BURNETT: Correct. I wasn't able to find anything, and we received nothing to indicate.

DR. BELSITO: So, basically, we don't have 28-day dermal tox for leaf, stem, root, or sprout. They're not GRAS, so those would be insufficient.

DR. LIEBLER: Right. I agree.

DR. BELSITO: And I thought the HRIPT for the distichon covered the vulgare, but -

DR. SNYDER: I said yes, unless Don says there's issues with barley sensitization.

DR. BELSITO: No, I mean, yeah, there's IgE-mediated hypersensitivity. We deal with that with all the grains, but, okay.

And, I just had a question, Christina, on Table 3, PDF 30. It says cultivar one and cultivar two. Does this represent the distichon versus the vulgare, or different cultivars of one of them?

MS. BURNETT: I believe it's different cultivars of one of them.

DR. BELSITO: And we just don't know which one.

MS. BURNETT: It's vulgare according to the reference.

DR. BELSITO: Okay, so we should just put that maybe in the title?

MS. BURNETT: Okay.

DR. BELSITO: So, basically, we have safe as used for whatever and insufficient for the leaf, stem, root, and sprout-derived ingredients for 28-day dermal, is that correct?

DR. LIEBLER: That's right.

DR. BELSITO: Any other comments?

DR. LIEBLER: So our seed ingredients are fine. Non-seed ingredients, insufficient.

MS. BURNETT: Yes. We did a similar approach with the wheat ingredients.

DR. LIEBLER: Yeah.

DR. ANSELL: And we still have that botanical statement that we addressed earlier.

DR. BELSITO: Yeah. And make the change in the -- that would be in the discussion, correct, Jay?

DR. ANSELL: Yeah.

DR. BELSITO: In the introduction.

DR. LIEBLER: Yeah.

DR. BELSITO: So that would be PDF page --

DR. ANSELL: Twenty-one.

DR. LIEBLER: Third paragraph after the ingredient list.

DR. BELSITO: Yeah.

MS. BURNETT: I did, for this team, have a question as to if you like Table 4, and if you like Table 4, do you have any suggestions on how it could look prettier?

DR. BELSITO: What PDF is that? What page, Christina?

MS. BURNETT: I'm sorry, it's PDF page 31. It was inserted in response to a request.

DR. LIEBLER: It's full of chemicals and numbers, what could be prettier than that?

DR. BELSITO: I guess, the only thing I'd --

MS. BURNETT: It's that kind of thing.

DR. BELSITO: Yeah, well, I mean, it's just obviously where there's nothing we don't have data. I didn't quite understand what the checks meant.

MS. BURNETT: It means that it was present, but I have no quantification.

DR. BELSITO: Okay, and we --

DR. LIEBLER: Yeah, just add a footnote, so it's clearer what that means.

DR. BELSITO: Yeah.

MS. BURNETT: All this data is also already presented in the composition and impurities section of the report.

DR. SNYDER: For me, I always love tabulated data better than narrative.

MS. BURNETT: Okay.

DR. BELSITO: Me too.

DR. LIEBLER: Yeah. So it's okay to leave it in. The narrative's also fine.

DR. BELSITO: Okay. Any other comments on barley? Okay.

Cohen's Team Meeting – September 13, 2021

DR. COHEN: Okay. Barley. So barley-derived ingredients. This is a draft tentative report. At the December meeting, we issued an IDA and asked for 28-day dermal tox on the whole plant of distichon and vulgare. And, if positive, we would look for reproductive and genotox. And dermal irritation data on max use for the whole plant for distichon and vulgare. We have max use for the vulgare at 1.5 percent in the leave-on and 1.8 percent for the distichon.

We had an ocular in-use study in HRIPT on a mascara containing 0.3 for the distichon and that was okay. And then we had a 2.76 percent for the distichon and 0.1 percent for the vulgare. That looked okay, although the max use for vulgare is much higher. And I don't think we got 28-day dermal tox.

DR. SHANK: Correct.

DR. COHEN: So what's the feeling of the group?

DR. SHANK: We still need the 28-day dermal and the skin sensitization for the distichon is okay, but not for the vulgare. So we need 28-day dermal and skin sensitization at 1.5 percent for the vulgare.

DR. BERGFELD: It's a GRAS item. Why do we need all that tox data on all these? On the vulgare? "It's safe on animals, drugs, feeds, and related products." For humans' consumption, it's made into a pearl barley. This is for non-cosmetic use.

DR. PETERSON: Is it because it's animal?

MS. BURNETT: The concern was with the non-edible parts, correct? The roots? The stem?

DR. SHANK: Correct. That's right.

MS. BURNETT: We had a similar issue with wheat, if you recall. And the Panel concluded with wheat to say the edible portions, the seed portions, were safe. But the inedible ones, without the GRAS data were not.

DR. BERGFELD: That's a good way to go.

MS. BURNETT: If that's what you would like.

DR. COHEN: That was the conversation we had last time was the non-edible components of it. And I still think that's where we stood last time. Tom?

DR. SLAGA: No, I agree with Ron, especially, on the non-edible.

DR. SHANK: Yeah, you can't use GRAS for the non-edibles.

DR. COHEN: What's the impact of animals eating -- are animals eating the whole plant?

DR. BERGFELD: Yes.

DR. SLAGA: Yeah, they eat the whole plant. So it's edible in a cow.

DR. PETERSON: But you know you can't draw a cross because there's certain plants that we can eat that are toxic to animals and vice versa. But I agree with what Ron and Tom have said so far.

DR. COHEN: Okay. So we have insufficient data. We need 28-day tox on distichon and vulgare. I don't think we have it for either one.

Now, I guess the question is this issue of read across, right? It's not really a read across. But if we had dermal tox on one, would we be satisfied for the other?

DR. SHANK: No, because apparently there's wide variation in the composition between the cultivars.

MS. BURNETT: But that data that is in that table, that is specific for the vulgare species. It's a sub-cultivar of that. Let me see what table that is. That would be PDF page 30.

DR. SHANK: Thirty?

MS. BURNETT: Yes.

DR. COHEN: Is that Table 3? Phenolic composition?

MS. BURNETT: Table 3. Yes. So that is two different cultivars of Hordeum Vulgare. I will correct that title.

DR. COHEN: They really are different, those two cultivars.

MS. BURNETT: Mm-hmm.

DR. SHANK: So the difference between distichon and vulgare is probably important.

DR. COHEN: Right. Okay. And so we'll ask for sensitization and irritation on vulgare and max use. Looks like we have distichon data.

DR. SHANK: Yes.

DR. COHEN: Got it. All right. I imagine this will be quite a discussion tomorrow. We'll see how that plays out.

DR. HELDRETH: So, for this report, then, since we're in a draft tentative stage, there's two options when you have data needs. If the data needs are the same as they were when the initial IDA was put out, then you can put out a draft tentative report with insufficient conclusion. But, if your data needs are different in any way from what was issued in the IDA, then you have the opportunity to put out a second IDA.

What I'm feeling these data needs are -- like, I mean, we can take away data needs. Let's say you didn't need the 28-day dermal anymore, but you still needed the DART study, the genotox study, you could go forward with an insufficient data conclusion. But, if there is something newly added, then you're going to want to forward with another IDA.

DR. COHEN: I don't think it's an IDA. It looks like this is a continuation of the existing data request.

DR. BERGFELD: This is December 20, 2020.

DR. COHEN: Yeah.

DR. HELDRETH: Right.

DR. SHANK: (Inaudible).

DR. HELDRETH: So then the usual step would be to issue a tentative report with an insufficient data conclusion for those ingredients.

DR. COHEN: I think that is how we have to land on this insufficient data conclusion because there's been no change in what we asked for.

DR. SHANK: Correct.

DR. COHEN: All right.

MS. BURNETT: So that's for all the ingredients? Or is that only for the non-seed ones? As it's written in the insufficient data announcement, you mentioned if you can get food-use evidence for the flowers, leaf, seed, and root since we didn't receive that, then it could be specifically geared toward those. And/or the whole, I guess, if you didn't get the data you needed for one of the whole plant extracts, that too.

DR. COHEN: That's a very provocative question.

MS. BURNETT: Sorry.

DR. COHEN: Well, because we have sensitization data on distichon, and there are edible parts of it, right?

MS. BURNETT: Of the seed, yes.

DR. COHEN: Of the seed. So would not those be eligible to pass through?

MS. BURNETT: There's only two -- is there only two distichon? I'm sorry. I don't know how to say it myself.

DR. COHEN: Yeah.

MS. BURNETT: Dr. Belsito says it completely different. I can't even say it the way he says it.

DR. COHEN: Distichon or something like that? Or --

MS. BURNETT: He pronounces it more like Italian or Spanish.

DR. COHEN: All right. Well, we'll have Brooklyn meet that tomorrow.

DR. SHANK: Are we supposed to laugh when that comes up tomorrow?

MS. BURNETT: I don't know.

DR. COHEN: Yes, when the laugh and applause signs go up, you just respond.

MS. BURNETT: I think he says, "di-sti-chon". He breaks it up more phonetically, I guess.

DR. COHEN: So the seed, the distichon seed flower, could we not move that along? We have the extract -- Lisa, the extract would cover the seed and the extract?

DR. PETERSON: I would think the flower, for the seed flower, would cover the extract in the water. You know, I guess I'm just -- sorry, there's a bunch of things that we don't have any information on -- no reported use on. Could we -- you know, it gets to the same conversation that we had earlier.

DR. COHEN: That sounds like it's something we're going to be doing in the future --

DR. PETERSON: Oh, okay.

DR. COHEN: -- in the near future, but this is what's sort of in front of us now.

DR. PETERSON: Right. Well, I think the seeds stuff is probably all fine.

DR. COHEN: You're talking about for distichon?

DR. SHANK: Yes.

DR. COHEN: We don't have tox or max use irritation sensitization for vulgare which is the lion's share of that table.

DR. PETERSON: Yeah, you do have -- isn't there sensitization on the vulgare seed extract?

DR. COHEN: There's a vulgare extract at 0.1 percent.

DR. PETERSON: Does that not go high enough?

DR. COHEN: And it's 1.5 percent for the vulgare extract as max use. It's over an order of magnitude difference.

DR. PETERSON: Yeah. Okay. I think for the seed vulgare -- anything seed related -- you can from the --

DR. COHEN: I think it's just the distichon, right?

DR. PETERSON: Yeah.

DR. COHEN: We still need sensitization and irritation for vulgare across the board, right? Ron, is that how you read it?

DR. SHANK: Yes. Yes, that's right.

DR. COHEN: Yeah, but do we have a safe-as-used for the distichon extract and the seed flower? Will the extract cover the seed flower? That's my question. I didn't -- I wasn't prepared to answer that.

DR. SHANK: I would think so.

DR. COHEN: Is the extract the whole plant?

DR. HELDRETH: Yes, according to the definition.

DR. COHEN: So it looks like the distichon could pass muster here. Any objections to that? So we can have safe-as-used for the distichon extract and seed flower? And insufficient data conclusion for vulgare?

DR. PETERSON: For all of the vulgare?

DR. SHANK: Yeah, we don't have anything for vulgare.

DR. BERGFELD: Leaf or seed.

MS. BURNETT: But even for the seeds?

DR. SHANK: Seed extract.

MS. BURNETT: Because that is the one that would be GRAS. That's the barley you eat.

DR. COHEN: So the vulgare, you're saying seed extract, right?

MS. BURNETT: Just, generically, barley seeds. Vulgare would be the most widely used of the barley species.

DR. COHEN: So we have use of them. We don't have max percentage, max concentration.

DR. BERGFELD: You have that. In vulgare, in your table, you have a 0.1 percent, 50 patients HRIPT, no sensitization, no irritation. It's seed extract. And then on your table of "Duration of Exposure," the rinse offs are at 1.5 max. And the rest of them in other applications are in a point 0 something.

DR. COHEN: I see that's the distichon, right. So you have leave-ons at 1.5 percent --

DR. BERGFELD: Yeah, but that's --

DR. COHEN: -- the vulgare.

MS. BURNETT: No, that's the whole plant extract. Correct.

DR. COHEN: And then we don't have any concentration of use for the leaf, the seed extract, or the seed flower, even though they're used.

MS. BURNETT: Correct.

DR. COHEN: Wilma, that's where I'm kind of wrapped around the axle.

DR. BERGFELD: Okay.

DR. COHEN: On the Vulgare 1.5 percent max use and the data at 0.1, right? So --

DR. BERGFELD: Yep. Well, you can go ahead and ask for it, but you also have to ask for the leaf and the seed extract that you have listed right there in that table because you have nothing. And I think that you have in this testing --

DR. COHEN: Let me go back down.

DR. BERGFELD: Yeah, they're all extract. The only one that was seed extract was the 0.1.

DR. COHEN: Yeah, the highest vulgare work we see is 0.1.

DR. BERGFELD: In the seed extract.

DR. COHEN: In the seed extract. So, we're over an order of magnitude different.

MS. BURNETT: Right.

DR. COHEN: And the vulgare extract, in my mind, would cover all the rest of them if we had some max use work there.

DR. BERGFELD: Right.

DR. COHEN: We could at least get seed flower, seed extract through if we had that. So is this a split conclusion?

MS. BURNETT: Sounds like it.

DR. HELDRETH: It sounds like it.

MS. BURNETT: So you're saying safe as used for the dichi -- distichon, distichon two ingredients and then insufficient for the remaining?

DR. COHEN: Yeah.

MS. BURNETT: Okay.

DR. COHEN: Is that satisfactory to the team for now?

DR. SHANK: Yes.

DR. HELDRETH: Yes.

DR. COHEN: Okay.

MS. BURNETT: Bart, is this the new IDA? Or is this the tentative3?

DR. HELDRETH: It depends what the data needs are.

MS. BURNETT: Okay.

DR. HELDRETH: Are you saying it's the same as the IDA?

DR. COHEN: Yes.

DR. HELDRETH: So previously issued?

MS. BURNETT: Okay. So it would be a tentative conclusion.

DR. HELDRETH: Tentative, right. Yes.

DR. COHEN: Insufficient data conclusion?

DR. HELDRETH: Split conclusion of safe for the two distichon and then insufficient for the remaining ingredients. And then in the discussion the data needs would be there, and they would need to be the same as the previous IDA.

MS. BURNETT: Got that.

DR. BERGFELD: So it wouldn't be an IDA conclusion; it would be a tentative final, wouldn't it?

DR. HELDRETH: A tentative report, yes.

MS. BURNETT: A tentative report.

DR. BERGFELD: A tentative report.

MS. BURNETT: So in addition to that paragraph spelling out the needs, are there any other discussion items that need to go into the report that aren't already highlighted?

DR. COHEN: I don't think so.

DR. SHANK: Do you want to point out the variation between the cultivars in the discussion?

MS. BURNETT: We could do that.

DR. BERGFELD: That's a good idea.

MS. BURNETT: And before we move away, I wanted to get the Panel input on Table 4. If that looks okay? If there's any way to make it look prettier?

DR. COHEN: Are you talking about the composition one?

MS. BURNETT: Yes. I do know I need to define what the check marks mean. So I need to add that as a footnote, but if there were any other suggestions to this table?

DR. SHANK: It's pretty enough.

DR. COHEN: There's so many lines on it. There's just so many components.

MS. BURNETT: Correct. Okay. As long as you're satisfied with the way it looks.

DR. BERGFELD: What was the discussion about the checkmarks? Are you just getting the actual?

MS. BURNETT: Checkmark, I just didn't put a footnote to define what a checkmark means. The checkmark means that it exists. Some report says this composition exists, but I wasn't given the details as to how it was in any quantity.

DR. BERGFELD: Okay. So are you going to fill that in then? Or are you not going to fill that in? You just going to do an asterisk?

MS. BURNETT: I'll put a footnote defining what the checkmark is. I don't have any data as to what the quantities are.

DR. BERGFELD: Okay. Okay.

Full Team Meeting – September 14, 2021

DR. COHEN: This is a draft tentative report. At the December 2020 meeting the panel issued an IDA, and the additional data for the 16 ingredients were a 28-day dermal tox on the whole plant extract for Distichon -- and we had a discussion whether Don was calling it Distichon or Da-sheek-cun (phonetic), or something similar to that; we were going to find out -- and Vulgare. And we wanted irritation and sensitization data at max use on the whole plant extract for both species, or both plants. We came to a split conclusion, safe as used for Hordeum Distichon Extract and Seed Flour, insufficient data conclusion on Vulgare. We still needed a 28-day dermal tox and sensitization and irritation at max use. That's a motion.

DR. BERGFELD: A second or a comment, Don?

DR. BELSITO: We came to a slightly perhaps different conclusion. We thought that the seed ingredients were safe as used, the non-seed were insufficient. And we're not sure what is GRAS and what is not GRAS, so that was one of the insufficiencies was in determining the GRAS status of the non-seed components. And we thought the HRIPT was okay for the Distichon but not the Vulgare.

DR. COHEN: All right, so, those are similar conclusions. So, what Vulgare parts did you clear?

DR. BELSITO: The Vulgare parts that we cleared were the Seed Extract, the Seed Flour, and the Seed Water.

DR. COHEN: And, the HRIPT on those were very low concentrations despite Vulgare having a 1.5 percent leave-on, and I think the sensitization data was a .005 and .1. So, we didn't know if we had bridged that gap. And since the differences in the cultivars were so great, we thought we wanted closer sensitization data than what we were provided for the Vulgare.

DR. BELSITO: I didn't really see anything in the composition of the cultivars that raised my antennas for sensitization. So, again, it's an issue with my using expert opinion despite the fact that we didn't have a specific HRIPT at max concentration of use. I mean, looking at this I'm not seeing anything that really is concerning to me.

DR. COHEN: I can buy that. So, for Seed Extract, Seed Flour and Seed Water, your feeling is we have all the necessary tox because it's GRAS.

DR. BELSITO: Right.

DR. COHEN: And, the HRIPT was good enough.

DR. BELSITO: Based upon the known composition of two different cultivars.

DR. COHEN: Okay. Ron, Tom, Lisa, any thoughts with going with that?

DR. SHANK: That'd be okay. You have to put that in the discussion.

DR. SLAGA: Okay here.

DR. PETERSON: Fine with me.

DR. BERGFELD: Any other comment, David, because I'd like Don to repeat his motion. Don?

DR. BELSITO: So the Hordeum Vulgare Seed Extract, Seed Flour and Seed Water are safe as used. All of the others are insufficient for determination of GRAS status, and if not GRAS, other systemic toxicity endpoints such as a 28-day dermal may be needed. So basically what we're saying right now is the others are insufficient primarily for systemic endpoint.

DR. COHEN: What about the two Distichon?

DR. BELSITO: Yeah, the Distichon is -- right. So the other components of the Vulgare -- so the Extract, the fa-da-da and the Distichon are insufficient.

DR. COHEN: Can you just clarify why the Distichons were insufficient?

DR. BELSITO: The Distichon Seed Flour was sufficient as well. Is that correct, Dan?

DR. LIEBLER: That's correct. It's the Distichon Extract, which is a whole plant extract, that's the problem. We're okay on the seed ingredients across both Vulgare and Distichon, the problem is anything other than seed-derived stuff, we don't have food use, or we don't have evidence of GRAS.

DR. BERGFELD: That clarifies it?

DR. COHEN: I would second that motion.

DR. BERGFELD: Okay, and we heard that some of this material that we've just discussed will come into the discussion. Okay. And the needs will be listed. All right, any other things to be commented upon or editorials to be brought forth? Hearing none, I'm going to call the vote. All those opposed? Abstaining? Unanimous approval of the safe and the insufficient report on Barley.

Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Status: Draft Final Report for Panel Review
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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.

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 that 4 barley-ingredients (i.e., the seed-derived ingredients) are safe in cosmetics in the practices of use and concentration described in this safety assessment. However, the Panel also concluded that the available data are insufficient to make a determination that the remaining 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations.

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 Vulgare Leaf/Stem Powder
Hordeum Distichon (Barley) Seed Flour	Hordeum Vulgare Powder
Hordeum Vulgare Extract	Hordeum Vulgare Root Extract
Hordeum Vulgare Flower/Leaf/Stem Juice	Hordeum Vulgare Seed Extract
Hordeum Vulgare Juice	Hordeum Vulgare Seed Flour
Hordeum Vulgare Leaf Extract	Hordeum Vulgare Seed Water
Hordeum Vulgare Leaf Juice	Hordeum Vulgare Sprout Extract
Hordeum Vulgare Leaf Powder	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. Thus, in this assessment, the Panel is evaluating the potential toxicity of each of the barley-derived ingredients as a whole, complex substance; toxicity from single components may not predict the potential toxicity of botanical ingredients.

Many of the barley-derived seed ingredients in this safety assessment (as well as the germinated and dried grain known as malt) 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 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 route⁶ or by inadvertent ingestion from cosmetic products to precipitate a flare-up of either gastrointestinal or cutaneous symptoms.⁷ The Panel has reviewed the safety of hydrolyzed wheat gluten as used in cosmetics and concluded that this ingredient is safe when formulated to restrict peptides to an average molecular weight of 3500 Daltons or less.⁸

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.

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.^{9,10} 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.^{1,10} 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.^{1,11,12} In present day, it is cultivated on all continents, except Antarctica, in temperate and tropical areas.¹³

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).^{1,14} Barley sprouts are the young leaves of barley harvested approximately 10 d after sowing seeds.¹² 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 - 4.7.¹⁵ 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.¹⁶

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.¹⁷ 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.¹⁸ 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.¹⁹ 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.²⁰

Another supplier has reported that *Hordeum Vulgare* Seed Extract is produced by harvesting hydroponically cultivated barley seeds, then drying and milling them.²¹ 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.²² 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).²³⁻²⁵ 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.²⁶ Table 3 describes the phenolic composition of three different parts of two different barley cultivars.²⁷ 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.^{9,24} Phytochemicals in barley grain include phenolic acid, flavonoids (flavanols, anthocyanins, proanthocyanidins), lignans, tocopherols, phytosterols, and folates.²⁸

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.¹⁰ The main species affecting harvests are *Alternaria* spp., *Helminthosporium* spp., *Fusarium* spp., *Cladosporium* spp., *Aspergillus* spp., and *Penicillium* spp.¹⁰ 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 *Penicillium*.^{10,29,30} As a point of reference, the Panel has adopted the United States Department of Agriculture (USDA) guidelines corresponding to “negative” aflatoxin content in nuts and grains.³¹

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.¹⁷ 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%.³² 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 μ g/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.³³

Hordeum Distichon (Barley) Seed Flour

Acetone extracts of *Hordeum distichon* grains contain 5-*n*-alkylresorcinols.²³ 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.³⁴ 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, flavanols, tannins, triterpenoids, and vitamin C.³⁵ 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.³⁶ 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.³⁷ 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.³⁸ 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.³⁹

Another supplier has reported that the composition of a *Hordeum Vulgare* Seed Extract tradename mixture also contains sodium chloride and tromethamine.¹⁶ At 1 ppm of the seed extract, there is approximately 0.038% tromethamine. No further detail on constituents was provided. Levels of the pesticides avermectin and pirimicarb were below level of detection.⁴⁰

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.⁴¹ 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.⁴² 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.¹²

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.⁴³ 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.⁴⁴ 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).⁴⁵ *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.⁴⁶ 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.⁴⁷ 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 6.⁴⁵⁻⁴⁷

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.^{46,47} 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.⁴⁶ 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.^{48,49} 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.^{50,51} 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.⁵²⁻⁵⁴

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.⁵⁵

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.^{1,14} 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.¹⁰ 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.^{1,10}

Barley has been used in traditional medicine to treat various inflammatory and cardiovascular diseases.⁵⁶ 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.^{35,36,57,58} Barley seed flour applied topically has been studied for therapeutic benefits in infants with jaundice.⁵⁹ Barley grass (in powder form) has been described as a developing functional food with novel preventive drug potential.⁶⁰ Young barley grass water and juice extracts have been studied for obesity inhibition³⁴ and chemopreventative potential in human colon and lung cancer cell lines,^{61,62} while young green *Hordeum vulgare* leaves have been studied for anti-stress properties that could be beneficial in treating psychiatric disorders such as depression.⁶³ Barley sprout “essence” and extract has been studied for its effects on blood cholesterol and treatment for chronic alcohol-induced liver injury.^{12,64-66}

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 (n = 20), while a mascara containing 0.3% *Hordeum Distichon* (Barley) Extract had “negligible” irritation potential in a 14-d cumulative irritation assay (n = 25).^{67,68} A mascara product containing 0.3% *Hordeum Distichon* (Barley) Extract was determined to not be sensitizing in a human repeated insult patch test (HRIPT; n = 111), but low-level (±) reactions were observed in the induction and challenge phases.⁶⁹ No dermal sensitization was observed with a lotion containing 1.8% *Hordeum Distichon* (Barley) Extract in a HRIPT (n = 102); however a slight potential for dermal irritation was noted.⁷⁰ *Hordeum Distichon* (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8% (n = 54);⁷¹ however, one subject (n = 49) 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.⁷² No dermal irritation or sensitization were observed in HRIPTs of a

pressed powder (n = 107), a facial moisturizer (n = 101), or a facial mask (n = 110) each containing 0.005% *Hordeum Vulgare* Extract, or in a skin serum formulation (n = 50) containing 0.1% *Hordeum Vulgare* Seed Extract.⁷³⁻⁷⁶

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

Hordeum 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.⁷⁷ 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.⁷⁸ 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.⁷⁹ 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.⁸⁰ 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.⁸¹ 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.⁸²⁻⁸⁵ 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.^{82,84,85} 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.^{82,84,85} 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.⁸³ 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.⁸⁶⁻⁸⁸ Food allergy to barley has been reported; in Korean children, evidence of cross-reactivity or co-sensitization with wheat has been found.^{89,90}

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 ailments.

Many of the barley-derived seed ingredients that are reviewed in this safety assessment, as well as malt, 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. *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.

DISCUSSION

The Panel reviewed the safety of 16 botanical ingredients derived from the barley plants *Hordeum distichon* and *Hordeum vulgare*. The Panel concluded that the available data are sufficient for determining safety of 4 ingredients, i.e., those derived from barley seeds, as reportedly used in cosmetics. The Panel noted that the barley seed-derived ingredients that are reviewed in this safety assessment are found in foods that may be consumed daily, and daily exposure from food use would result in much larger systemic exposure compared to that resulting from use in cosmetic products. Additionally, 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 fact, coupled with negative findings in human dermal irritation and sensitization studies on whole plant extracts and seed extracts, led the Panel to determine that barley seed-derived ingredients are safe for use in cosmetic products.

The Panel noted that constituent yields can greatly vary between species cultivars, and even between parts of the same plant. While seeds of barley are generally recognized as safe (GRAS) for food use, other barley plant parts are not GRAS for food use, and safety test data are lacking. Thus, the Panel also concluded that data are insufficient for determining the safety for the non-seed ingredients. The additional data needed to determine safety of these ingredients as used in cosmetics 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 use as a food for ingredients derived from the flower, leaf, stem, and root.

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 USDA guidelines corresponding to “negative” aflatoxin content in nuts and grains.

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

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 4 barley-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

Hordeum Distichon (Barley) Seed Flour*
Hordeum Vulgare Seed Extract

Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water*

**Not reported to be in current use. Were ingredients in this group not in current use to be used in the future, the expectation is that they would be used in product categories and at concentrations comparable to others in this group.*

However, the Panel also concluded that the available data are insufficient to make a determination that the following 12 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Hordeum Distichon (Barley) Extract
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 Sprout Extract**
Hordeum Vulgare Stem Water**

***There are currently no uses reported for these ingredients.*

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, <i>Hordeum distichon</i> .	Skin-conditioning agent – misc.
Hordeum Distichon (Barley) Seed Flour	Hordeum Distichon (Barley) Seed Flour is the flour obtained from the finely ground seeds of <i>Hordeum distichon</i> .	Abrasives; bulking agent
Hordeum Vulgare Extract 85251-64-5	Hordeum Vulgare Extract is the extract of the whole plant, <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Juice 85251-64-5	Hordeum Vulgare Juice is the liquid expressed from <i>Hordeum vulgare</i> .	Not reported
Hordeum Vulgare Leaf Extract 85251-64-5	Hordeum Vulgare Leaf Extract is the extract of the leaves of <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Leaf Juice 85251-64-5	Hordeum Vulgare Leaf Juice is the juice expressed from the leaf of <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	Antioxidant
Hordeum Vulgare Powder 85251-64-5	Hordeum Vulgare Powder is the powder obtained from dried and ground whole plant, <i>Hordeum vulgare</i> .	Abrasive
Hordeum Vulgare Root Extract 85251-64-5	Hordeum Vulgare Root Extract is the extract of the roots <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Seed Extract 85251-64-5	Hordeum Vulgare Seed Extract is the extract of seeds of <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	Skin-conditioning agent – misc.
Hordeum Vulgare Sprout Extract 85251-64-5	Hordeum Vulgare Sprout Extract is the extract of the sprouts of <i>Hordeum vulgare</i> .	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 <i>Hordeum vulgare</i> .	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 *Hordeum vulgare* cultivars.²⁷

Phenolic Compounds	Cultivar 1			Cultivar 2		
	Leaves	Seeds	Stems	Leaves	Seeds	Stems
3- <i>O</i> -feruloylquinic acid	39.8	NR	5.8	4.3	NR	5.1
chlorogenic acid	NR	NR	1.1	NR	NR	0.8
luteonarin	2150.8	1.5	NR	760.8	NQ	NR
<i>p</i> -coumaric acid	NR	6.2	5.3	NR	3.4	18.6
isoorientin-7- <i>O</i> -rutinoside	208.4	NR	NR	68.5	NR	NR
luteolin-6- <i>C</i> -arabinoside-8- <i>C</i> -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- <i>O</i> -[6-feruloyl]-glucoside-4'- <i>O</i> -glucoside AND apigenin-6- <i>C</i> -arabinoside-8- <i>C</i> -glucoside	30.9	7.3	3.4	14.2	6.4	5.4
isovitexin-7- <i>O</i> -rutinoside AND isoscoparin-7- <i>O</i> -glucoside	217.5	29.3	8.8	70.5	26.4	15.3
apigenin-6- <i>C</i> -glucoside-8- <i>C</i> -arabinoside AND isovitexin-7- <i>O</i> -[6-sinapoyl]-glucoside-4'- <i>O</i> -glucoside	14.3	0.4	NQ	7.9	0.2	NQ
isoscoparin-7- <i>O</i> -rutinoside AND isoorientin	87.6	1.7	1.1	52.3	4.5	1.5
isovitexin-7- <i>O</i> -[6-feruloyl]-glucoside-4'- <i>O</i> -glucoside	3.1	NR	NR	3.1	NR	NR
isoorientin-7- <i>O</i> -glucoside-4'- <i>O</i> -[6-feruloyl]-glucoside AND isoorientin-7- <i>O</i> -[6-caffeoyl]-glucoside AND chrysoeriol-6- <i>C</i> -glucoside-8- <i>C</i> -arabinoside AND isoscoparin-7- <i>O</i> -[6-sinapoyl]-glucoside-4'- <i>O</i> -glucoside	32.6	NR	NR	23.1	NR	NR
isoorientin-7- <i>O</i> -[6-sinapoyl]-glucoside	167.3	NR	NR	47.8	NR	NR
isoorientin-7- <i>O</i> -[6-feruloyl]-glucoside-2''- <i>O</i> -glucoside AND isoscoparin-2''- <i>O</i> -glucoside AND isovitexin	3.2	NR	NR	2.0	NR	NR
isoorientin-7- <i>O</i> -[6-feruloyl]-glucoside	494.6	NR	NR	74.8	NR	NR
isovitexin-7- <i>O</i> -[6-sinapoyl]-glucoside	18.2	NR	NR	2.5	NR	NR
isovitexin-7- <i>O</i> -[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) ^{32,33}	Hordeum Distichon (Barley) Seed Flour ²³	Hordeum Vulgare Leaf Juice ³⁴	Hordeum Vulgare Seed Extract ³⁵⁻³⁷	Hordeum Vulgare Seed Flour ⁴¹	Hordeum Vulgare Sprout Extract ^{12,43,44}
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 quercetin equivalents/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			√			

√ denotes component presence, but quantification was not available.

Table 5. Frequency (2021)⁴⁵ and concentration (2018;⁴⁶ 2020⁴⁷) of use according to duration and type of exposure for barley-derived ingredients

	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>	<i># of Uses</i>	<i>Max Conc of Use (%)</i>
	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
<i>Duration of Use</i>								
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
<i>Exposure Type</i>								
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
<i>Hordeum Vulgare Seed Flour*</i>								
Totals[†]	2	NR						
<i>Duration of Use</i>								
Leave-On	1	NR						
Rinse Off	1	NR						
Diluted for (Bath) Use	NR	NR						
<i>Exposure Type</i>								
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.⁴⁵⁻⁴⁷

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	Dose	Test Population	Procedure	Results	Reference
IRRITATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	0.05 ml applied	25 subjects	14-d cumulative irritation assay; test article applied via 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	⁶⁸
Product containing 0.005% Hordeum Vulgare Extract	Amount applied not reported	20 subjects	48-h patch test; test article applied via 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	⁶⁷
SENSITIZATION					
HUMAN					
Mascara containing 0.3% Hordeum Distichon (Barley) Extract	0.05-0.10 g	111 subjects	HRIPT; test article applied via 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	⁶⁹
Lotion containing 1.8% Hordeum Distichon (Barley) Extract	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	⁷⁰
Eye cream containing 1.8% Hordeum Distichon (Barley) Extract	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	⁷¹

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

Test Article	Dose	Test Population	Procedure	Results	Reference
Facial moisturizer containing 2.76% Hordeum Distichon (Barley) Extract	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	⁷²
Facial moisturizer containing 0.005% Hordeum Vulgare Extract	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	⁷⁵
Facial mask containing 0.005% Hordeum Vulgare Extract	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	⁷⁶
Pressed powder containing 0.005% Hordeum Vulgare Extract	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	⁷³
Skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract	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	⁷⁴

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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