
Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

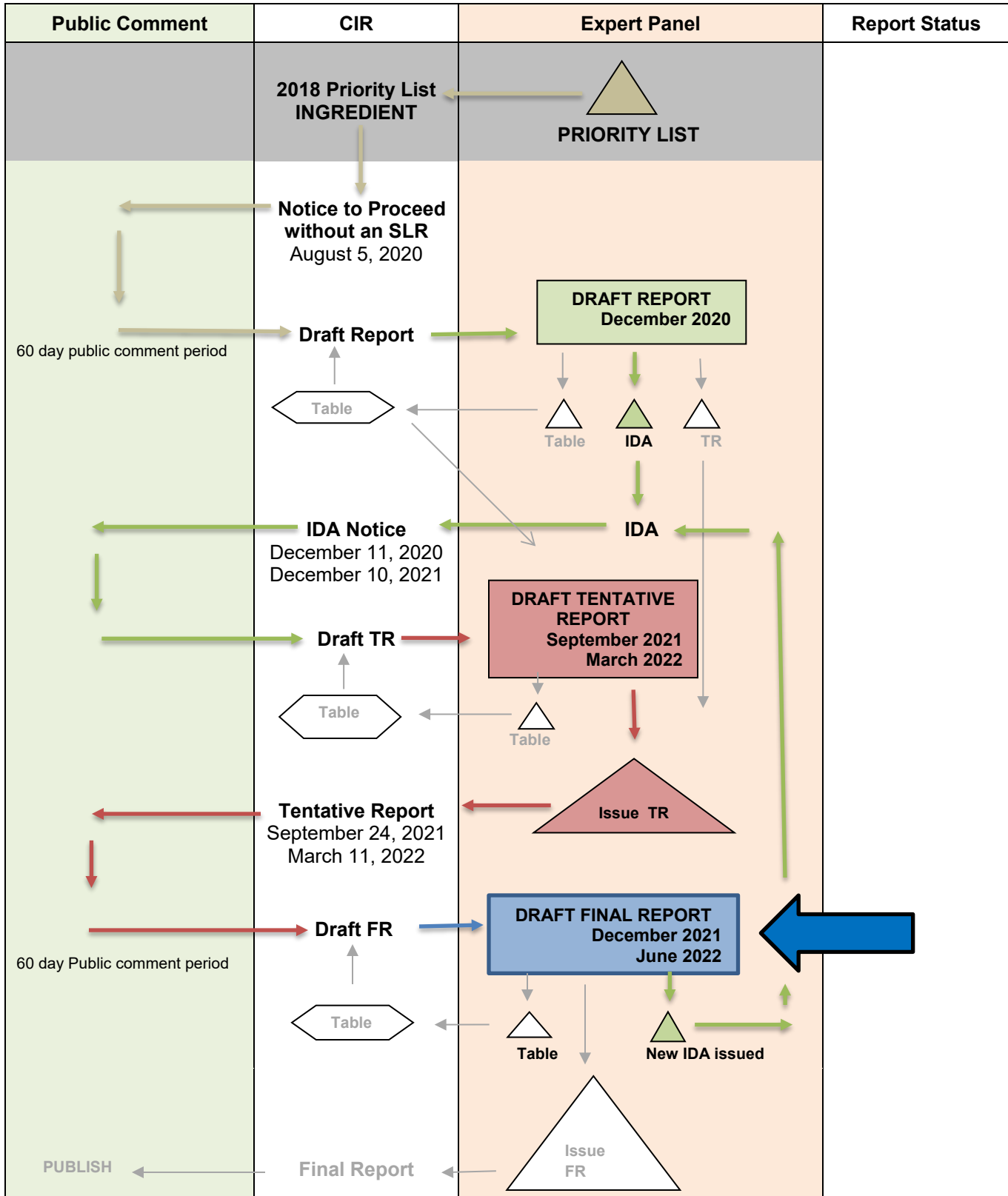
Status: Draft Final Report for Panel Review
Release Date: May 23, 2022
Panel Meeting Date: June 16-17, 2022

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.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; Susan C. Tilton, Ph.D. Previous Panel member involved in this assessment: Lisa A. Peterson, 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 June 2022





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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst, CIR
Date: May 23, 2022
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_062022* in the pdf document.) At the March 2022 meeting, the Panel issued a Tentative Report with the conclusion that the 5 barley seed- and sprout-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 11 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:

- Explanation of the plant parts used to make the whole plant extracts *Hordeum Distichon* (Barley) Extract and *Hordeum Vulgare* Extract
- Method of manufacturing for *Hordeum Distichon* (Barley) Extract and *Hordeum Vulgare* Extract
- Composition and impurities data for *Hordeum Distichon* (Barley) Extract and *Hordeum Vulgare* Extract
- 28-day dermal toxicity data on the whole plant extract *Hordeum Distichon* (Barley) Extract and *Hordeum Vulgare* Extract
 - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
 - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for *Hordeum Leaf* Extract, or other leaf ingredients

Since the issuance of the Tentative Report, CIR has received no new unpublished data. The attached Council comments on the Tentative Report have been addressed (*PCPCcomments_Barley_062022*), as noted in the check sheet immediately following the comments (*response-PCPCcomments_Barley_062022*). Changes to the language involving the inhalation exposure boilerplate and use in airbrush delivery systems have been highlighted to aid the Panel's review.

Additional supporting documents for this report package include a flow chart (*flow_Barley_062022*), report history (*history_Barley_062022*), transcripts (*transcripts_Barley_062022*), search strategy (*search_Barley_062022*), data profile (*dataprofile_Barley_062022*), and 2022 VCRP data (*VCRP_Barley_062022*).

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: March 23, 2022

SUBJECT: Tentative Report: Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics (release date March 11, 2022)

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

Introduction – Please revise: “as well as the endpoints that Panel typically evaluates” (add “the”)

Composition/Impurities – Please revise: “Mycotoxins produced by these fungi and bacteria” (delete bacteria, because all the species listed in the previous sentence are fungi, and mycotoxins by definition are produced by fungi)

Ocular Irritation: Summary – It is misleading to state that there are no ocular irritation studies. This section and the Summary should refer to in-use studies of eye area products that assessed irritation.

Summary – In the Summary, it would be helpful to note that although the ingredients named without a plant part are defined as whole plant preparations, suppliers have indicated that they may be made from the seed. Please correct “various part have been” (add “s” to part)

Table 3 – Please define NR at the end of the table.

Table 4 – Please define DM and GAE at the end of the table

Table 7 – Please correct: “several drop of water” (add “s” to drop)

Barley-Derived Ingredients – June 2022 – Christina Burnett	
Comment Submitter: Personal Care Products Council	
Date of Submission: 3/23/2022	
Comment	Response/Action
Introduction - Please revise: “as well as the endpoints that Panel typically evaluates” (add “the”)	Correction made.
Composition/Impurities – Please revise: “Mycotoxins produced by these fungi and bacteria” (delete bacteria, because all the species listed in the previous sentence are fungi, and mycotoxins by definition are produced by fungi)	Corrected to read “Mycotoxins produced by fungi...”
Ocular Irritation: Summary – It is misleading to state that there are no ocular irritation studies. This section and the Summary should refer to in-use studies of eye area products that assessed irritation.	Ocular Irritation section deleted and Summary updated.
Summary – In the Summary, it would be helpful to note that although the ingredients named without a plant part are defined as whole plant preparations, suppliers have indicated that they may be made from the seed. Please correct “various part have been” (add “s” to part)	Suggestion was not used. Only one supplier indicated that the ingredient labeled as a whole plant extract was made with seeds due to antiquated naming system. We do not know if this applies for all suppliers of this ingredient. Correction made.
Table 3 – Please define NR at the end of the table.	Correction made.
Table 4 – Please define DM and GAE at the end of the table	Correction made.
Table 7 – Please correct: “several drop of water” (add “s” to drop)	Correction made.

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.

December 2021 - the Panel issued a new IDA. The additional data needed to determine safety of these ingredients as used in cosmetics are:

- Clarification of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract

- Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
 - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
 - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for Hordeum Leaf Extract or other leaf ingredients

December 20, 2021 – Additional unpublished data received.

March 2022 - The Panel issued a Tentative Report with the conclusion that the 5 barley seed- and sprout-derived ingredients are safe as used in cosmetics in the present practices of use and concentrations described in this safety assessment.

The Panel noted that the barley seed- and sprout-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- and sprout-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 remaining 11 barley-derived ingredients.

The additional data needed to determine safety for these cosmetic ingredients are:

- Explanation of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
 - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
 - Alternatively, acceptable evidence of safe use as food for ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for Hordeum Leaf Extract, or other leaf ingredients

Barley-Derived Ingredients Data Profile* - June 2022 - 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
Hordeum Distichon (Barley) Extract	X		X	X																X		X							X
Hordeum Distichon (Barley) Seed Flour			X	X																									
Hordeum Vulgare Extract	X		X	X																X		X							X
Hordeum Vulgare Flower/Leaf/Stem Juice																													
Hordeum Vulgare Juice				X																									
Hordeum Vulgare Leaf Extract	X													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

Updated search on 4/29/2022 yielded no additional relevant references.

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

LINKS**Search Engines**

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

appropriate qualifiers are used as necessary

search results are reviewed to identify relevant documents

Pertinent Websites

- wINCI - <http://webdictionary.personalcarecouncil.org>
- FDA databases <http://www.ecfr.gov/cgi-bin/ECFR?page=browse>
- FDA search databases: <http://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm234631.htm>;
- Substances Added to Food (formerly, EAFUS): <https://www.fda.gov/food/food-additives-petitions/substances-added-food-formerly-eafus>
- GRAS listing: <http://www.fda.gov/food/ingredientspackaginglabeling/gras/default.htm>
- SCOGS database: <http://www.fda.gov/food/ingredientspackaginglabeling/gras/scogs/ucm2006852.htm>
- Indirect Food Additives: <http://www.accessdata.fda.gov/scripts/fdcc/?set=IndirectAdditives>
- Drug Approvals and Database: <http://www.fda.gov/Drugs/InformationOnDrugs/default.htm>
- FDA Orange Book: <https://www.fda.gov/Drugs/InformationOnDrugs/ucm129662.htm>
- (inactive ingredients approved for drugs: <http://www.accessdata.fda.gov/scripts/cder/iig/>)
- HPVIS (EPA High-Production Volume Info Systems) - https://iaspub.epa.gov/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 Panel 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 flour, two total uses. One with being generically described as barley flour. 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 flour, 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 flour, for the seed flour, 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 flour? Will the extract cover the seed flour? 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 flour? 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 flour, 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 flour, 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 Panel 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.

DECEMBER 2021 PANEL MEETING – 3RD REVIEW/DRAFT FINAL REPORT

Belsito's Team Meeting – December 6, 2021

DR. BELSITO: At the September meeting, we issued a tentative report with a conclusion that the four barley seed-derived ingredients are safe in cosmetics in the present practices of use and concentration. We also concluded that the available data were insufficient to make a determination about the remaining 12 barley-derived ingredients, and the additional data was a 28-day dermal tox on the whole plant extracts, Hordeum Distichon extract, and Hordeum Vulgare extract. If positive, tox studies and genotox data may be needed. Alternatively, if there was evidence that these components of barley were used in foods, we would reconsider that need.

There was no new unpublished data provided, and there was updated information regarding gluten content in cosmetics and use of barley grass developing functional foods that were added to the report. There was some council input. The CIR staff noted a quote from a celiac disease researcher that "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 was no reference. Should this information be added to the report, and should there be a damaged skin caveat? We can discuss that.

Let's look at the report. In terms of that comment from that celiac disease individual, glutens are proteins. I don't think there'd be significant absorption even if there was stratum corneum disruption. It would be sort of similar to what we looked at with the PEGs, that you'd almost had to have full thickness for it to be a problem. I'll open it up for comments from the team members.

DR. LIEBLER: I agree with what you just said. I think there's just nothing to cite here. I certainly wouldn't support going as far as a damaged-skin caveat in the conclusion. I think this is a nonissue. I don't disagree with the celiac disease researcher. It doesn't really need to be mentioned.

DR. BELSITO: Paul, Curt?

DR. SNYDER: Yeah, I don't think we need to go there unless we had data that suggested there was a product that was intended to be used on damaged skin.

DR. BELSITO: Right.

DR. KLAASSEN: I agree. No comment.

DR. BELSITO: Okay, so we just don't mention it or even mention the damaged skin. Then, I'm not following on PDF page 38, "this barley grass in powder form has been described as a functional food with novel preventative drug potential." Where is barley grass fitting into this?

DR. SNYDER: What page are you on because it only goes to 28? You said 38.

DR. BELSITO: PDF page 38 on barley --

DR. SNYDER: Oh, I'm sorry.

DR. BELSITO: -- under non-cosmetic use.

MS. BURNETT: How that fits into the report?

DR. BELSITO: Yeah. What is barley grass?

MS. BURNETT: I believe it'd be the same as a leaf powder or leaf extracts, leaf juice. They don't call it grass. They call it the leaves.

DR. BELSITO: Right. That's what I was sort of presuming.

DR. SNYDER: We received the comment from the PCPC stating that the barley grass is a food, a.k.a. the leaves.

DR. BELSITO: Okay.

DR. SNYDER: We just have to have that clarified in the report, that the barley grass is the leaf.

DR. BELSITO: That's our assumption. We don't know.

DR. SNYDER: PCPC sent us comments I have on my notes regarding that issue of the barley grass equals food, a.k.a. the leaves.

DR. BELSITO: Is that in Wave 2?

DR. SNYDER: No, that would've been right at the beginning, under that table that we get now, which I think is very, very useful. I really appreciate that, moving that upfront, because that helps.

MS. BURNETT: It would be PDF page four and five. Yeah, four and five.

DR. LIEBLER: On PDF 38 under non-cosmetic use, the end of that first paragraph might be the place to add a sentence to state that barley grass is a food form, if I got that correct, Christina?

MS. BURNETT: I'm sorry. Repeat that.

DR. LIEBLER: Barley grass is a food form, is that right?

MS. BURNETT: Yes. Yes, it is.

DR. LIEBLER: Maybe we could add a short sentence at the end of the first paragraph under non-cosmetic because you say, "barley for human consumption is made into pearl barley by using abrasive disks," blah, blah. And then you can say "barley grass is a food form of barley."

MS. BURNETT: Okay.

DR. LIEBLER: Then, when we refer to barley grass down below, there's no ambiguity. Where is this coming from?

DR. BELSITO: Okay, you have that, Christina? Otherwise, I was okay with the conclusion and the discussion.

DR. SNYDER: Me too.

DR. LIEBLER: I agree.

DR. BELSITO: Curt?

DR. KLAASSEN: Yes, fine.

DR. BELSITO: Okay.

Cohen's Team Meeting – December 6, 2021

DR. COHEN: So, barley, we came in safe for four of the seed-derived ingredients and insufficient for 12 ingredients. We asked for 28-day dermal tox on whole plant extracts of distichon and vulgare, and if positive, we'd ask for further -- we'd ask for DART and genotox. Alternatively, we would be interested in hearing about it as a food. That might reduce our need for that.

Since that report we've -- I don't think there's much there. There was a question from Christina about the celiac disease use and the irritation, which seemed consistent with our wheat-derived product report.

DR. BERGFELD: Right. I thought that was an important statement, myself.

DR. COHEN: Hmm?

DR. BERGFELD: I thought that was an important statement regarding the protein.

DR. PETERSON: Yeah, and there actually is a reference. If you go to the website that is linked, there's a reference in the -- yeah, the council's letter has a website. And if you click on that website, it gives the statement of the doctor about this statement about celiac's disease. And then that statement on the website is referenced. And I put the reference in my PDF copy that I'll send along, but basically, it's dealing with the Academy of Nutrition and Dietetics 2012 reference.

DR. COHEN: And what did specifically it say? Because it's very hard to find references on this.

DR. PETERSON: Yeah. It basically says that, you know, because gluten isn't absorbed -- I mean, the problem with gluten is that, when it gets, in it causes problems and -- for people who have celiac's disease. But if it stays on the outside of the body, it shouldn't be a problem. And the only way it can get in is if the skin is damaged, and then it can get into the bloodstream. But this reference actually deals with that whole issue, I believe, when I looked at it. I looked at it just briefly, but it seemed to be a good reference for that particular statement.

DR. COHEN: From a completely experiential and practical standpoint, it's what we tell -- tend to tell patients.

DR. SLAGA: In general.

DR. COHEN: Yeah.

DR. SHANK: But is this relevant? It has to be broken skin and --

DR. PETERSON: Or abrasive, you know, skin that's abraded, you know -- the skin has to be damaged.

DR. SLAGA: Yeah.

DR. SHANK: Yeah, well, we could probably consider that in every ingredient.

DR. SLAGA: Right.

DR. SHANK: If the ingredient is put on damaged skin, then there may be different problems.

DR. PETERSON: Right.

DR. SHANK: I wouldn't pick it out just for this one.

DR. COHEN: Ron, this comes up as a matter of practical issue for gluten-sensitive patients. It's a specific call-out. It's less a toxicologic thing than it is a pseudo-allergic thing. I take your point, abraded skin's going to allow percutaneous penetration for most things.

DR. SHANK: Right.

DR. COHEN: But this comes up from a consumer perspective a lot, right? Not the absorption of glucosamine through damaged skin or radish extract, but this particular one.

DR. SHANK: Okay.

DR. BERGFELD: But there are case reports that talk about contact urticaria to barley. It's under case reports, clinical studies.

DR. COHEN: Yeah.

DR. BERGFELD: It didn't say it was damaged skin, there were urticaria. Usually in damaged skin you get a --

DR. COHEN: It comes around a fair amount. So, would this allow us to bring in some of the leaf components as safe?

DR. BERGFELD: I don't know if that's declared as a food, barley grass.

DR. COHEN: It's on WebMD. It's on a number of sites espousing the value of eating barley grass.

MS. BURNETT: It's similar to wheatgrass that they, you know, use. They juice it. You add it to your smoothie.

DR. COHEN: So, all right. But maybe taking that out of the equation for now, what are the comments about this report moving along? Lisa, do you want to make some comments?

DR. PETERSON: Well, I have one comment. I think I was -- I thought it was good to go. You know, I agreed with the conclusion. And I thought that the information about the gluten and celiac's disease should be included, and I had the reference. That's the extent of my comments on this. I think it's basically ready to go.

DR. COHEN: So, just for clarity, we had insufficient data for 12 ingredients looking for more tox information. And --

DR. PETERSON: Yeah, and then they'd just be -- well --

DR. COHEN: You're maintaining the insufficiency.

DR. SLAGA: Right. We have no new data so we have to --

DR. PETERSON: We have no new data, so I thought -- yes, I thought that it was safe for the ingredients we previously said it was safe for. It was insufficient for the insufficient ones. I was fine with the conclusion as it's stated.

DR. SHANK: I agree.

DR. SLAGA: I agree.

DR. COHEN: So, you are not persuaded that the leaf extract, leaf juice, and leaf powder cannot move any further because of its use as food?

DR. SHANK: Correct.

DR. BERGFELD: What is a malt extract?

DR. COHEN: That was the -- that was the last thing. That's a sort of -- they take the seeds, and they let them germinate. And then they stop it.

DR. PETERSON: I think the problem is that you're missing -- you know, the leaf is gonna be different than the seed. And you're missing irritation, sensitization, that kind of stuff. It's not that it's probably not systemic, but there's no irritation/sensitization data for those. We only have it for the seed. We don't have it for the leaf. And so, you know, it's different eating it versus putting it on your skin. So that's why.

DR. COHEN: Just remind me, Lisa, the extract -- the vulgare extract, is that the whole --

MS. BURNETT: So --

DR. COHEN: -- that's not whole plant, that's just the seed?

MS. BURNETT: The hordeum vulgare extract is a whole plant, not just a seed, and then there's separate hordeum vulgare seed extract.

DR. COHEN: The sensitization is on distichon extract. Distichon extract. Okay. So, if the leaf -- so you're not satisfied with the leaf extract, the juice, or the powder being food, would we still need the tox on it, or are we just going to have now sensitization and irritation on it?

MS. BURNETT: You do have HIRPTs on both the whole plant extracts for both species.

DR. COHEN: We have for both species. We have seed for vulgare, and we have -- yeah, yeah, so --

MS. BURNETT: It bleeds onto the next page, right? It's PDF pages 38 and 39.

DR. COHEN: All right. So if we have that, then why are we not clearing leaf extract, juice, and powder? Just talk me out of it for a moment.

MS. FIUME: Is it because the distichon and vulgare extract themselves are insufficient? They were not found sufficient. Only the seed ingredients were found sufficient.

DR. PETERSON: Yeah, I think.

MS. BURNETT: So the insufficiency there was the 28-day dermal tox for the whole plants.

DR. COHEN: Right. So, do we need 28-day dermal tox for this?

DR. SHANK: They're not foods, so --

DR. COHEN: Well, the --

DR. SHANK: -- we can't dismiss it because they're foods.

DR. COHEN: Well, the leaf is food.

DR. SHANK: Is it?

DR. COHEN: Well, the grass is eaten, and the grass and the leaves are synonymous, apparently.

DR. SHANK: Well, the report says the leaf is not food. So, if you now have data that it is, we have to change that in the report.

DR. ANSELL: Yeah, the barley sprouts and barley grass are eaten.

DR. COHEN: So, Jay, you're saying they are food?

DR. ANSELL: Yeah, that's my notes, that the barley sprouts and barley leaves are eaten. Comment provided with the tentative report.

MS. BURNETT: In the non-cosmetic use section, I added a reference that says that the barley grass in powder form has been described as a functional food.

DR. COHEN: Right.

MS. BURNETT: It's being used in studies as -- for novel drug studies, and already it's used in juice bars to supplement smoothies. But there is no other, you know, authoritative source that says this is a food item.

DR. SHANK: Well, if you're going to say they're foods, then we have to change the report.

MS. BURNETT: Right.

DR. SHANK: Because in the discussion it says they're not food and, therefore, we need toxicity data.

DR. ANSELL: Some inconsistency within the reports, Christina?

DR. SHANK: And in any case, none of them are GRAS.

MS. BURNETT: The --

DR. SHANK: Foods are not GRAS. Food additives are GRAS.

DR. SLAGA: Right.

DR. SHANK: Or can be.

MS. BURNETT: I'm sorry, I'm a little confused. So, the sentence that I added was new since the discussion was created by the Panel at the last meeting.

DR. SHANK: Okay.

MS. BURNETT: And it's just one sentence that was added to the non-cosmetic use section. So, when the discussion was created at the time --

DR. SHANK: Okay.

MS. BURNETT: -- the Panel was under the belief that the leaves were not consumed, that they were not --

DR. SHANK: Okay. Let me find that.

DR. COHEN: It's under non-cosmetic use in the third paragraph.

MS. BURNETT: It's the highlighted sentence.

DR. COHEN: That sentence is what is provoking this discussion. And I don't know what level of authoritative information we need to call something a food, but it's widely -- it's on WebMD as people eating it. It's out there as food. So, I don't want to hold something up that doesn't need to be held up.

DR. SLAGA: Well, if that is sufficient data to call it food in a food class, then we have to go with safe, right?

DR. SHANK: Yes.

DR. SLAGA: I mean, that's -- we don't need anything else. It doesn't have to go insufficient. If that -- if there is references that define the grass and the leaves as really food, then we're safe.

DR. COHEN: So, I might suggest it was the leaf extract, leaf juice, leaf powder. There is one item that's leaf stem and I didn't know what to make of that one.

DR. BERGFELD: Well, it would go with the extract -- with the whole plant.

DR. SLAGA: Yeah, it's eaten.

DR. COHEN: Okay. Then --

MS. BURNETT: The sprout probably is the same as grass.

DR. SLAGA: Yeah.

DR. ANSELL: Well, and this is entirely consistent with the data deficiency report that alternatively acceptable evidence for use of a food for ingredients derived from flower, seed, stem, or root.

DR. COHEN: Right. So, it opens up -- we asked for -- in the IDA, we asked for information. We kind of have information that it's -- we have the alternative pathway fulfilled, which is food. I don't know what to make of the root, but --

MS. BURNETT: I mean, I think -- I can't remember exactly, and I'm looking it up right now. But at the end, I think, with the wheat report we also moved the leaves to the safe category at the end because of the anecdotal it's used in juicing or whatever and a similar type reference. I'm trying to pull it up to verify.

DR. COHEN: Well, if we have the whole plant extract dermal sensitization and we have food. I don't know if we shouldn't just come out with a safe as used for the whole thing.

DR. SHANK: I agree.

DR. BERGFELD: Who has to put the rubber stamp on it, it's a food, it's GRAS? Is that (inaudible) or can it just be in the literature?

MS. BURNETT: I don't know.

DR. COHEN: Well, Ron has eaten the foot-long radish so -- or, Tom has eaten the foot-long radish, so does that count?

MS. BURNETT: All right. So, I have the wheat report pulled up, and in the end you guys said flour, germ, seed, bran, and gluten were safe. But you kept the leaf extract, peptide, the stem water, proteins, sprout, and straw water in the insufficient category.

DR. COHEN: And what was it insufficient for?

MS. BURNETT: I'm sorry, I just closed it. Hold on, I accidentally closed it.

DR. COHEN: Look, I also think in this particular situation, not being a long-hauler here, I do get the sense that these botanicals require a lot of evolution in the way we think, and they weren't the typical process for the group. So, I understand that we might have some inconsistencies in the short-term until we come to an agreement on this.

MS. BURNETT: All right. The insufficiency was composition and impurities data. And if it was significantly different, then you wanted dermal irritation and sensitization data at maximum use concentration. That's what that was. I mean, there was different -- obviously we had different data needs filled in different areas between the two reports.

DR. PETERSON: Yeah. And we don't have any composition -- we have composition for the barley extract but don't have any composition for --

DR. COHEN: And what do we need from that? If this is a food, do we need that if we have a boilerplate --

DR. PETERSON: It's tells you --

DR. COHEN: -- for the pesticides?

DR. PETERSON: -- it tells you that -- whether they're similar -- how similar or different they are in terms of their chemical composition. And that allows you to draw conclusions about their -- you know, if you can see the composition and you compare it to the barley extract is a whole plant.

DR. SHANK: But if they're food what difference does it make?

DR. PETERSON: Because you're worried about the sensitivity. I mean, that's my understanding. It's not the health part. It's the sensitivity. And you don't have irritation/sensitivity for those things. That's --

DR. COHEN: We --

DR. PETERSON: -- that's my understanding of why they would be insufficient is because you -- can you draw across the line, you know, that the composition is more or less the same?

DR. COHEN: I think we do have sensitization.

DR. PETERSON: I mean, this gets into the same precise conversation we had about looking at an ethyl versus an ethyl extract of a plant. Because different things are there, and one was potentially harmful. And the other wasn't. And it gets into what are the composition differences and the things that we think might be responsible for any sensitization? So, I think that -- I think that's how come we ended up with wheat the way we did, if I'm remembering that conversation correctly.

So, if one draws a parallel to that conversation to this, we didn't do wheat that long ago. So, you know, there hasn't been any breakthrough science that's different that I'm aware of that's happened since we discussed the wheat. So, I would take the same tact with barley. And I think that's where -- why Tom and -- I guess I shouldn't speak for them, but that's kind of how I reacted to it is like, okay, it's food, but still we're missing these things. You don't know.

MS. BURNETT: We do have Tables 3 and 4 that do show some of the composition of the leaves compared to the seeds and the stems.

DR. COHEN: We do have sensitization data on distichon. We have sensitization data on vulgare, I think, at 0.1 percent, which is below max use. But we have distichon sensitization data at over max use.

DR. BERGFELD: I think with the uncertainty we go for the insufficient ask.

DR. COHEN: Okay. All right. So what are we asking for as insufficient? In our IDA in September, we asked for dermal tox of the whole plants for distichon and vulgare -- said, alternatively acceptable evidence of use as a food derived from the flower, leaf, stem, and root. So, I guess the group has to say we're not persuaded by the fact that people eat this.

DR. SLAGA: No.

DR. COHEN: And we're going back and saying what? We want more evidence it's a food, or we want the tox? It's going to be a difficult discussion tomorrow. I just need some help getting through this.

DR. SLAGA: Well, if it's a food, we don't need the tox if we have -- we don't need any systemic tox anyway.

DR. COHEN: The only thing I can --

DR. SLAGA: Just sensitization.

DR. COHEN: The sensitization at max use for vulgare, right?

DR. SLAGA: Right.

DR. COHEN: It's the only thing I could see that we don't have in light of us asking -- issuing the IDA last time.

MS. FIUME: So, David, there's actually a tentative report that went out last time, and this would be a final report.

DR. COHEN: Oh, yeah, this is a draft final report.

MS. BURNETT: And that would be a new data need, so it would go back as -- Monice, wouldn't it go back --

MS. FIUME: I'd have to look and see what was asked for before because if they don't -- if they're not becoming -- if they stay the way they are, the report can probably go out as it is if you're not persuaded that it's a food. The other item to think about as you're talking about it, if you're persuaded that the leaves are food but you don't have any food information on the flower, stem, or root, what would make those switch over to the safe categorization, even if you decided to move the leaf ingredients?

DR. COHEN: Probably the same provisions, right? Either the tox or the evidence of being food.

MS. FIUME: Okay. So, they wouldn't be able to switch from insufficiency; is that correct? Because you don't have any evidence that these are foods.

DR. ANSELL: Yeah, we do have that.

MS. FIUME: Not for the flower, leaf -- the flower, stem, and root.

DR. ANSELL: But the extracts we do -- whole plant extracts.

MS. FIUME: But the whole plant extract is currently insufficient, Jay.

DR. ANSELL: Right. But the sufficiency was redressed by demonstration that it's a food and FDA lists it in their list of foods. So, I think --

DR. BERGFELD: Is that correct?

DR. ANSELL: Yeah.

MS. FIUME: The malt extract is listed as a food.

DR. ANSELL: Right.

MS. FIUME: Barley grain is used for food.

DR. COHEN: Well, the malt extract is the plant sprouting, and then they stop the growth after it sprouts, correct?

MS. FIUME: Mm-hmm.

DR. COHEN: So, it's the whole plant. It's just the little one.

DR. PETERSON: Yeah. But, I mean, you can't make that argument because the --

DR. COHEN: Yeah, I --

DR. PETERSON: -- gene expression and then the metabolites are going to be so different.

DR. COHEN: Yes.

DR. PETERSON: And, you know, it's just like a baby fetus has different things (inaudible).

DR. COHEN: Yes, yeah.

DR. ANSELL: You know, it's not malt sprout --

DR. COHEN: I wanted to take that back as I said it.

DR. ANSELL: It's malt syrup and malt extract which are listed as the foods.

MS. FIUME: And while you're discussing that, that actually leads into another question that has kept coming up in the comments. And Christina, I'll let you go ahead and address that because I know you wanted to get to it at some point, but it seemed to open the door.

MS. BURNETT: So, both in the introduction and in the introduction to the toxicity study section, we have that -- let me see. I have it highlighted somewhere -- that the barley seed ingredients as well as the germinated dried grain known as malt may be consumed as food. It's not -- the malted barley is not an ingredient in this report, but we mention malted barley. Do we want to keep reference to malted barley in the report, or do we need to take it out? Since the last iteration I have defined what malt is a little bit better so that it's clear as to what it is, but we are not reviewing malted barley.

DR. COHEN: What drove the reason to define it?

MS. BURNETT: It was a council comment, I believe, on PDF page 4. "If the term "malt" is going to be left in the report, it should be defined."

DR. COHEN: And if the term isn't in there, we don't need to discuss it at all.

MS. BURNETT: Correct. But it also removes the -- it probably means that we should remove the reference of the GRAS status of malted barley then. I'm unsure what to do with that. I mean, if including anything that refers to malted barley in the report adds confusion, then maybe it should be removed, including the GRAS status.

DR. COHEN: Tom?

DR. SLAGA: I say leave it in. It adds something to it.

DR. PETERSON: I mean, it was the first thing that came to my mind when I was looking at barley. I was like, oh, malt. So, I actually agree with leaving it in because it just sort of clarifies it's a different thing. And yes, we've done it -- I mean, we reviewed it separately.

DR. COHEN: I'm okay with that. Ron.

DR. SHANK: I don't think it makes much difference. If it's not an ingredient, I would leave it out so it doesn't get mistakenly included.

DR. COHEN: So, we have two ins and an out.

DR. PETERSON: I switch to an out.

DR. COHEN: Okay.

DR. SLAGA: It's not a big deal -- out.

DR. COHEN: Okay. Okay. And now so back to the banal. What are we going to -- this is a final report. What are we -- what do we want as insufficient? Are we okay at least advancing the leaf products through and the sprout?

DR. BERGFELD: The extracts for sure.

DR. SHANK: Yeah.

DR. COHEN: Leaf extracts, leaf juice, leaf powder, leaf stem powder, and, yup -- those four? Well, let's see.

DR. BERGFELD: Probably all but the root.

DR. SHANK: Yeah, four. All but the root. Leaf extract, leaf juice, leaf powder, leaf stem powder.

MS. BURNETT: What do you think about sprout?

DR. SHANK: No, that would be a -- well, that's the -- is that a food?

MS. BURNETT: I am unable to tell you when they kind -- when they harvest the grasses that they consume for this -- for the tasting. But from experience with the wheat it's like little grass that's like yay-tall that they trim off and grind up right there in the store.

DR. COHEN: I don't want to throw another wrench in this, but isn't the sprout like the malt? Isn't it sprouted seed that's halted?

DR. SLAGA: Yeah. That's why I thought it should stay in.

DR. BERGFELD: I don't know.

DR. COHEN: You mean go forward, Tom, and pull it from insufficient and put it as safe?

DR. SLAGA: Right.

DR. COHEN: Anyone opposed to that?

DR. ANSELL: Could you say that again?

DR. COHEN: Yeah. So, look, we have the four barley seed-derived ingredients as safe. The rest -- the remaining 12 were insufficient, and we want a tox or food designation. We can't bring all 12 -- we can't bring everything forward as safe, but we felt there's enough evidence that leaf and sprout, which comprises five additional ingredients here, have enough information to bring them forward because they're food.

I guess the only thing I would say that I'm arguing with myself on is we don't have max use on vulgare extract. We have it in a low concentration. We have it in 0.1, not 1.8. Is that right, Christina? Did I -- we have vulgare at 0.1?

MS. BURNETT: In terms of supporting data? I'm sorry.

DR. COHEN: Yeah. Yeah, in terms of HRIPT.

MS. BURNETT: Okay. We have vulgare extract at -- or the distichon extract at 2.7 --

DR. COHEN: Right, but this is --

MS. BURNETT: -- and the other one at -- yeah, well, that's the seed extract at 0.1 percent. You have the whole plant extract at 0.005 percent.

DR. COHEN: The question is do we think that's an issue that would hold it up? I might mention just from a technical perspective that Belsito is presenting this one, and we can flex a little bit with how we do this. But I think there's some flexibility in the leaf and sprout on the group?

DR. PETERSON: Yes.

DR. COHEN: All right.

MS. FIUME: David, one other issue, not to complicate, but because this is a final report and any changes made in something like the discussion do need to be brought up in public session, Christina, is it correct that the second paragraph with the discussion on page 41 will need some wording changes? Because currently we're saying that barley is GRAS, and that's technically not correct.

MS. BURNETT: Correct. That will need to be fixed. I'm not sure if you could say just malted barley is --

DR. PETERSON: Well, seeds of barley are GRAS because that's what you eat -- that's what you cook, barley.

DR. COHEN: But it's food.

MS. BURNETT: It's food.

DR. PETERSON: Oh, it's food. Oh, I see.

MS. BURNETT: So, under GRAS that's like stuff that's approved for adding to food. Anything that's been eaten for a while is assumed to be safe.

DR. COHEN: Okay.

MS. BURNETT: So, I'm going to need a resummarization of all the things that we talked about because the Panel went back and forth. I'm sorry. One thing I have is that you want to add the celiac expert's quote to the introduction, correct?

DR. COHEN: We can agree to that.

MS. BURNETT: Okay. The malt, in or out?

DR. PETERSON: I think we decided in if the sprouts -- keep it in if we decided to keep the sprouts as --

DR. SHANK: Right.

DR. PETERSON: -- food, the sprouts were sufficient, safe.

MS. BURNETT: Okay. Out if it's not though.

DR. PETERSON: Yup.

DR. COHEN: Yeah. Okay. And we're positively disposed to pass the four leaves and the sprout pending the discussion tomorrow. We don't have HRIPT, but it's not the first time we haven't had max use sensitization on every single item.

DR. SHANK: Right.

DR. COHEN: And we can use our discretion to some degree on this. Notwithstanding some contact urticaria, it's not a product that comes up a lot in contact dermatitis discussions. So, Christina, are we okay to move on, or do we have to declare it?

MS. BURNETT: I don't know if you need to declare it. You have your talking points for tomorrow when Dr. Belsito speaks, and anything can change given what they present.

MS. FIUME: But just as a point of clarification, it will be able to go forward as a final report because it's becoming less restrictive. So even though the categorizations may change, it still will be able to be issued as a final report.

DR. COHEN: Right. The question will be --

DR. SHANK: We're changing the conclusion. We're changing the conclusion.

MS. BURNETT: But it would be less restrictive for those ingredients that are currently insufficient.

DR. SHANK: Okay.

DR. COHEN: It'll be fewer insufficient ingredients.

MS. BURNETT: Correct.

MS. FIUME: And then I think the discussion about the gluten and abraded skin would become an edit for the -- added to the discussion. It doesn't make the report more restrictive or anything like that. So, it should be able to go forward as a final.

DR. SHANK: Okay.

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DR. BELSITO: Yes. So in September 2021 we issued a tentative report with a conclusion that four barley seed derived ingredients were safe in cosmetics, present practices of use, but we also concluded the available data were insufficient to make a determination that the remaining 12 barley derived ingredients that were not seed were -- we could not determine whether they were safe under the intended concentrations of use. And the data we needed was 28 day derma-tox on the whole plant, both the hordeum distichon extract and hordeum vulgare extract and then a positive and development repo data, genotox data or alternatively to those data needs, evidence that those other barley ingredients were GRAS. We have no new unpublished data.

We had a comment about the gluten content of barley saying that it would not be a problem for individuals with celiac disease unless they had skin lesions. There were no references, and we were asked whether we should add that to the report. And my team felt a resounding no on that aspect.

In terms of the report itself, we agreed with the current conclusion, which was that the four barley derived seed ingredients are safe in cosmetics in the present practice of use and concentration, and that would be the seed flour, seed extract, seed flour for the vulgare as well as the distichon and seed water for the vulgare. And all of the non-seed ingredients which are listed in the report were insufficient for the needs that were previously mentioned.

DR. BERGFELD: And that's a motion?

DR. BELSITO: That's a motion.

DR. BERGFELD: Is there a second or a discussion?

DR. COHEN: Second with a discussion.

DR. BERGFELD: Okay. Go ahead.

DR. COHEN: So, Don, I think we had very similar discussions on our group, and from the last insufficiencies we had provided two pathways for fulfilling our insufficiency, which included acceptable evidence that some products were used as a food. There was an edit to the report indicating that the grass is eaten as a food, and it's widely discussed on the internet in a number of pretty reliable sites that barley grass is eaten as a food. I recognize that we have some HRIPT material on it and perhaps not at max use, and maybe using some experience we sought we might go safe as used for the four leaf products and sprouts since we considered those food products. We lack clarity on the roots.

DR. BERGFELD: But you did second the motion that was made, and now we're discussing perhaps reconsideration?

DR. COHEN: I'm sorry. Yeah, technically, yes, I guess I withdraw my second and just would rather have the discussion.

DR. BERGFELD: Discussion. Okay. Don, do you want to respond to that or Don's team?

DR. BELSITO: Yeah. We talked about that before on the leaf, and we determined not to conclude that at this point. I think we felt that there was not enough -- it was not grass. And there was not enough data, but I'll open that up to other team members.

DR. BERGFELD: Who would you like to call on?

DR. LIEBLER: Well, what do we have to cite for these food uses?

DR. COHEN: WebMD, a number of health sites discussing -- it wouldn't be grass. It's food, so it's widely out there using the grass to eat and to add into foods and shakes and things like that.

DR. BELSITO: Yeah. But so are a lot of nutritional supplements.

DR. COHEN: Yeah. When I put barley, grass, food, there's 55 million hits on that. Well, let me ask you guys. What do you need -- what makes you comfortable to feel that something is in fact a food?

DR. BERGFELD: Dan maybe?

DR. LIEBLER: I mean, I think we just missed this unless we talked about it and I don't recall. I don't remember anybody bringing up the food uses of barley grass on our team discussion.

DR. SNYDER: I mentioned that grass was the same as the leaf, but then we had further discussion that we weren't comfortable with the leaf, stem, and the roots -- I mean, the flower, stem, and the root. So I did mention that PCPC memo stating that the leaf was the same as the grass, so we did have a minor discussion about that.

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

DR. SHANK: Well, I don't have anything to add.

DR. SLAGA: I don't either.

DR. BELSITO: I guess my concern is for the grass we have the -- you know, we don't really have a lot of data, other than it's used as a food. We don't have that composition. We don't have -- we have some information about vulgare juice which comes from barley grass. There's a lot of data that we're missing on the grass aspect, even if we accept that it's food. And, you know, we don't know what's in it. We don't know sensitization and irritation for it. Is it different from the seed?

So I think even if we accepted it as food and dismissed the systemic toxicity, we don't have manufacturing. We don't have impurities. We don't have chemical composition, and we don't have sensitization and irritation. So I don't see how we can go safe as used for it.

DR. COHEN: Don't we have whole plant material on that? Christina, you were raising your hand.

MS. BURNETT: Yes, PDF page 43 on table 3 we do have some phenolic composition for the leaves and comparing between two cultivars.

DR. BELSITO: But that's it.

MS. BURNETT: Correct.

DR. COHEN: So, Don, if this was a well-established food -- if it was an apple, would you --

DR. BELSITO: I'd still have the same concerns, you know? I mean, just because you can eat the fruit, we don't know how the grass is prepared for cosmetics. Are there other things in there that would be of concern? What is the sensitization potential? We don't have that data.

DR. BERGFELD: Ron, do you want to comment? You talked about foods and grass and definitions yesterday.

DR. SHANK: Yeah. We shouldn't be -- when we say grass when you mean generally recognized as safe, GRAS with one S, that applies only to food additives, not foods. Now, barley grass spelled with two S's, we're told that that is a food, but we don't have any chemistry information on that. And the leaf and the root and that part of the plant apparently are not even used, so if we ask for that data, I don't think we're going to get any more. The only concern would be, I think, possible sensitization, and we don't have any information on that.

DR. COHEN: The extracts that we have, are those whole plants, Lisa? The distichon and the vulgare, those extracts, are those whole plants?

DR. SHANK: Yes.

DR. COHEN: We have sensitization data on that.

DR. LIEBLER: So what we've got is if they're eaten as foods, we normally don't worry about the systemic endpoints, and we focus on skin. And if we have sensitization data, we typically cleared ingredients that are food uses as long as they were clean on sensitization. I'm just looking at the table on PDF 46 and 47, which is the summary of the sensitization data, and it's hordeum distichon barley extract, barley extract, barley extract -- the first three entries for the HRIPTs. And then the next page, PDF 47, barley extract HRIPT, barley extract, barley extract, barley extract, and the last one is a seed extract. So most of the data is with the whole plant extracts. Just pointing that out.

DR. BERGFELD: So you're stating that we do have sensitization data on the grass --

DR. LIEBLER: It would appear so.

DR. BERGFELD: Don, do you want to reconsider your motion?

DR. BELSITO: I'm still having issues because we have whole plant, which is other than just grass. So the materials in the grass could be diluted. I mean, we don't even know how it's manufactured. There's absolutely nothing under method of manufacture for the grass. We don't know composition, and we don't know impurities. We'd never done this before for a botanical ingredient where we don't have that information.

DR. COHEN: So this is a final report; right? So if we go out with just what we had, we're limiting it to the seed materials.

DR. BELSITO: Correct.

DR. COHEN: And I think we thought we probably had enough to go out --

DR. LIEBLER: So we must be including the barley extract, aren't we? Or is it just the seed? Only seed?

DR. SHANK: Whole plant extract.

DR. LIEBLER: Yeah. The whole plant extract, it's got a bunch of uses.

DR. BELSITO: We asked for the whole plant. We asked for a 28 day dermal for both of them.

DR. LIEBLER: Yeah.

DR. BELSITO: And I think that --

DR. COHEN: Don, though, I think it read “alternatively acceptable evidence as use as a food from the flower, leaf, stem, and root.” I’m not suggesting we got all that from every one. I don’t think we have root, but the question at hand is, is there acceptable information about the leaf.

DR. BELSITO: But there’s not any use for the leaf. Oh, there is -- leaf extract, sorry. There are four uses and no reported concentration of use.

DR. COHEN: So just administratively if we carry the last motion, what happens to the rest of these? Because they are used. Do we come back to them, or this is it?

DR. BERGFELD: Bart, do you want to respond?

DR. HELDRETH: Sure. If the Panel concludes that a certain group of these ingredients are insufficient and it goes final, for two years that conclusion stays as is, insufficient data to conclude on safety for those ingredients. After the two year clock expires and no data has come in to fill the requested data gaps, those ingredients that have no uses will be removed to a category of zero use. And then those ingredients that have reported uses at that time will go into a new category called “use not supported.”

DR. BELSITO: Which means, unfortunately, that will be the majority because the majority of uses are for the whole extract, and that request I have to say came from the other team. So, David, why did your team change the need for the extracts?

DR. COHEN: Well, Don, I think when we gave the two pathways, we got one pathway back.

DR. BELSITO: Not for the whole extract. You got one pathway back for the grass, which is going to help you for, what, two ingredients out of the rest? I mean, the major ingredients are the extracts.

DR. COHEN: I think it’s three ingredients --

DR. BELSITO: It doesn’t matter. The bulk of the materials we’re looking here at are whole extract, which we’re not approving.

DR. LIEBLER: So maybe we need to table this and clarify the issue of whether the food uses are the whole plant, which can include leaves and stems. Seeds are already okay. I think you guys have pointed out -- the Cohen team has pointed out we’ve got barley grass uses as food. And now we’re kind of hung up on what about the rest of the plant? We don’t have the data on that, and I think trying to decide this on the fly is probably not wise, particularly when there are a lot of uses for the whole plant extract.

DR. BERGFELD: Is that something you would consider, Don? Because you have to rescind your motion.

DR. BELSITO: I mean, I think that if we’re going to get hung up about trying to approve the grass when we have no other data other than it’s reported use as food, which is only going to help us for a few of the ingredients -- and the bulk of the ingredients are with whole extract, yes -- when we look at the data again for the extract, we don’t have much information for the whole extracts either.

DR. COHEN: We have sensitization data on the extracts.

DR. BELSITO: We do, but we don't have -- I'm just looking. We don't have any information on chemical properties. We have some information on the distichon extract but otherwise not on the vulgare extract. We have composition and impurities for the distichon extracts and that's it.

DR. COHEN: We have vulgare seed flour, vulgare sprout --

DR. BELSITO: I'm looking at whole extracts, David. That's some major component here. We've already agreed that the seeds are okay. Yeah. We've gone through multiple iterations here, and we've not gotten the data. So we can table it, but are we going to get the data? We're going to have to come back and review this again. I mean, I think that we're all very cognizant of the information that we have right now, and we should try and make a decision because otherwise we're just going to be spinning the same wheels if we don't get any more data, which will --

DR. BERGFELD: We can table it with a proviso that we'll look at it the next meeting. Carol?

DR. EISENMANN: My observation is the data needs you listed in the tentative report were focused on systemic toxicity, and the data needs Dr. Belsito is asking for are focused on method of manufacture and chemistry. So there was a disconnect. You didn't really ask for what Dr. Belsito is now asking for, so if you want other data than what you've asked for, maybe you need to do another tentative report with different data needs.

DR. BERGFELD: Bart, can you --

DR. PETERSON: I agree with that because that is why we ended up going the way we did with the leaf yesterday because we went in a circle. And honestly, I'm looking at this now, and what you're asking for, Don, is not what we asked for.

DR. HELDRETH: Yeah. I agree that we do have a few options here. Certainly tabling is a potential option. However, typically when we table it's nice to see a deadline of here's the time when it's going to come back. And I'm not sure that the data is out there. I mean, Christina's already done a thorough search for what's available, so I don't know if tabling will actually get the Panel what they're looking for. However, if there are truly new data requests that were not in previous insufficient data announcements or even an insufficient data conclusion, then the panel does have the option to issue a new IDA -- a new insufficient data announcement.

DR. BERGFELD: Don?

DR. BELSITO: I mean, again, it was the other team -- I think we agreed to do 28 day dermal. I think our needs based upon what Dan usually asks for were probably manufacturing and impurities, which we don't have for one of the extracts. I mean, I think the more important -- if you look at use, the more important ingredients to get through are the extracts. Those are the ones that are used.

The seed and the grass have very small numbers of uses -- would be to get, you know, the method of manufacture. I need to go back to the table of which one we didn't get. We have method of manufacture for the distichon, so it would be the vulgare extract that we need. And for composition and impurities we have a whole lot on -- so different plant parts have different constituent compositions.

So I think that in terms of composition barley grain and then all the isotopes and stuff. We have composition and impurities on the usual botanical stuff for distichon. Seed flour, juice. Yeah, I mean, I would ask for the method of manufacture for the hordeum vulgare extract and manufacture and impurities for both extracts, and I think if we got those and had a sense -- composition would also be nice -- we could go ahead because we certainly have a lot of the HRIPT data. But the whole plant, these extracts are not foods.

DR. COHEN: Well, yeah. Perhaps we can get a little further information about the use of the whole plant as a food. At the group meeting, Don, you said -- so basically right now the others are insufficient primarily for systemic endpoints; right? So that's kind of how I felt we were guided through it and came to that conclusion because of the evidence about food. I appreciate you doing the insufficient data on it because I think maybe we can get a little further along next time.

DR. BERGFELD: So, Don, do I hear you right? You're going to go out for an IDA?

DR. BELSITO: That's what I would like to do if we want to see if we can increase the number of ingredients we're approving here.

DR. BERGFELD: So you're rescinding your original motion and making a motion to go out as an IDA?

DR. BELSITO: Yes.

DR. BERGFELD: Okay. Is there a second?

DR. COHEN: Second.

DR. BERGFELD: And the list -- Christina, do you have the list of what is being asked? I can't hear you. You're muted.

MS. BURNETT: I want to restate the list: method of manufacturing for the vulgare extract or for both extracts?

DR. BELSITO: We have method of manufacturing for the distichon I believe. Yeah, we have that so just the vulgare.

MS. BURNETT: Okay. And then composition and impurities for both whole extracts.

DR. BELSITO: Right.

MS. BURNETT: Do you still want the 28 day dermal that has not been received for the whole plant extracts?

DR. BELSITO: We could put that in, sure.

MS. BURNETT: Is that the three?

DR. BELSITO: Well, I guess since we're going out with an IDA I would ask if there's any information on sensitization and irritation for the grass.

DR. BERGFELD: Are you trying to exhaust the food use?

DR. BELSITO: Well, we've already exhausted the food use. I'll accept food use for grass, but as long as we're going out and asking for additional data, if they have sensitization -- well, not irritation because we could use the -- well, we really can't use the botanical boilerplate here because there are no substances of concern that we're aware of. Yeah. If they had sensitization and irritation for the barley leaf water, that would be good.

DR. SNYDER: But we need a clear definition of what the whole plant extract consists of. Does it include the root? Does it include the flower? Does it include the stem? Does it include the grass? I think that will help, and I think that's kind of where we got bamboozled here because there's multiple parts of the plant. And we're not certain which parts are in which ingredient classes here, so I think we want to be very, very clear because I think we were right before.

We said we wanted a 28 day dermal on the whole plant because they could clear the flower, the leaf, the stem and the root, or we wanted that it was a food ingredient. So I think that we've got to be very clear here, and if we get the method of manufacture, is it going to be sufficient for the distichon? Because we said the vulgare we're asking for, but I looked. I can't see here what even the hordeum distichon extract is comprised of.

DR. BELSITO: That's true.

DR. COHEN: Yeah, yeah. Good point.

DR. BERGFELD: So you're going to add both of them?

DR. BELSITO: Yeah. We might as well add it.

DR. BERGFELD: The whole plants and --

MS. BURNETT: For method of manufacture.

DR. SNYDER: I think a further comment to that is I think we've got to be careful that there's other -- food doesn't necessarily clear it because we have dermal exposure and the whole thing of sensitization and things are very important for cosmetics. So I think we've got to be careful about clearing things just because they're food.

DR. COHEN: Agreed.

DR. SNYDER: Systemic tox I agree, but we've got to remember that we can't lose sight of looking at mostly dermal exposures.

DR. LIEBLER: I completely agree with that, Paul. I also want to point out that the table that's currently in the report, table 3 on page 43, has for two cultivars broken down a list of phenolics for leaves, seeds, and stems. And what's interesting across the board is that leaves have the highest content of all the phenolics, higher than seeds and definitely higher than stems. So the leaves in a way could be considered most highly potent forms of the plant in terms of at least phenolic chemical constituents.

That would factor in at least to my thinking when we do have any further data on this to think about if leaves are food use and we have little concern about systemic toxicity with leaves, I wouldn't really balk at including a whole plant extract that contained leaf, seed, and stem based on the food use for leaves. I'm just sort of forecasting how I'm thinking about this. I don't know how Lisa would view it or any of the other people on the team, but anyway I just wanted to make that comment.

DR. BERGFELD: Any other comments about the proposed idea and what the use would be?

DR. BELSITO: So, Dan, from a dermo standpoint would you not be concerned that since the leaf is so compositionally different from the other parts that sensitization and irritation would be very important?

DR. LIEBLER: Oh, I think sensitization and irritation would be very important for the leaf, and in fact I think based on this table I think the leaf could clear the whole plant extract if you had it.

DR. COHEN: Yeah. The question is what proportion of the whole plant is leaf; right? Because, Dan, your point cut very deeply. It's a very important point, so if most of the plant substance is leaf, then the whole extract will be a pretty valuable piece of information from the sensitization standpoint. If it's not highly representative, then we might have an issue again.

DR. LIEBLER: No, I think that most of the plant's going to be leaves. I mean, a couple of photos might also help.

DR. BELSITO: And then I guess the other issue as Paul says is what exactly is the whole plant? Because the definition is the extract of the whole plant, but does it include the roots?

DR. BERGFELD: I think that's in the ask part of the IDA. Christina, did you add that?

MS. BURNETT: I'm sorry?

DR. BERGFELD: Did you add the fact that they want to know the actual parts of the plant that are in the extract, and does it include the root?

MS. BURNETT: We can ask that. I mean, based on the definition, it says whole plant, so I don't know how much clarification --

DR. BERGFELD: I guess it would be is the root in there because you would assume the stem and the leaves would be in there.

DR. BELSITO: These are the major uses. There's going to be obviously a manufacturer for these extracts that can tell us what they use.

DR. BERGFELD: Yeah. So let's go over the needs list, then, or what we're going to say. So, Christina, can you say it again? Can you list the needs?

MS. BURNETT: Method of manufacturing for the whole plant extracts, both of them, composition and impurities for both whole plant extracts, the 28 day dermal on the whole plant extracts, irritation and sensitization data for the leaf extract -- or leaf parts or confirmation of food use. Or do you still want that separate?

DR. BELSITO: Yeah. I don't think we need confirmation for food use at this point. We've got --

MS. BURNETT: Okay. And then if possible further explanation of what plant parts are actually in the whole plant extracts; is that correct?

DR. BELSITO: I wouldn't say "if possible." I mean, again, the major use -- the major part of the plant that's used is the whole plant extract, so there's got to be a manufacturer out there that can tell us do they dump in the whole thing or what are they throwing in when they make the extract?

MS. BURNETT: Okay. That's connected with the method of manufacturing.

DR. BELSITO: Yes.

MS. BURNETT: Okay.

DR. SNYDER: Maybe ask, Christina, do they pull up the roots? Do they just chop it off and take what's above ground, or do they pull it out of the ground?

MS. BURNETT: I mean, I don't know if they -- my Midwestern roots tell me they just mow it, but I'm used to seeing that used more for animal feed and stuff like that. I don't know if they yank it out anymore.

DR. BERGFELD: Okay. Well, we will receive that information hopefully. Now, I'm going to call the question on this because the motion's been made and seconded by David. All those opposed of moving forward as an IDA please state your name. Unanimously passed. Go ahead, Christina.

MS. BURNETT: So I do have two points I want to clarify before we move on. One team wanted to include the celiac expert's quote, and one team didn't.

DR. BELSITO: No.

MS. BURNETT: Can I have a consensus on that, please?

DR. COHEN: Yeah. Don's group, you said no. We hashed through it. We recognized the limited data on it but also probably the very high consumer interest in that specific issue, understanding that we can't address allergies in every circumstance of abraded skin or absorption. We just felt that this one was a somewhat unique circumstance, but we went back and forth on it, Don.

MS. BURNETT: There is a reference on the website that the council called our attention to that could possibly be used. I couldn't access the journal article, but that quote -- I did find that. In the reference I can't see anything that's -- they did not do any specific testing on abraded skin. They just kind of talk about an ELISA test. They didn't actually go in and test any rodents or human subjects, so I don't think it's a useful reference.

DR. COHEN: Don, did your group want it out for a specific reason?

DR. BELSITO: I don't think that we really have the data to support that one way or the other, but our feeling was that this is going to be something like the PEGS that we originally had not for use on damaged skin. And then we get all of this tape stripping data that showed that there was no significant absorption and that basically the renal issues that were seen with PEGS data were applied on third degree burns, and so our feeling was that we didn't want to even go into that aspect of it. Dan, maybe you can comment.

DR. LIEBLER: Yeah. So in short there's really no chance of significant absorption, and in the reference our sense was that there probably wasn't anything to cite. And Christina's just sort of confirmed that.

DR. BERGFELD: Okay. David?

DR. COHEN: Yeah. I think we're okay. Tom, Ron, Lisa, any objections to following Don Belsito's team's motion?

DR. SHANK: I support that.

MS. BURNETT: So I will leave it as it's written currently in the introduction. On the second point I needed to ask you about, I don't know if it was discussed in the Cohen's group, but we weren't able to discuss it in Belsito's group -- whether malt needs to stay in or out? And I realize there's an echo.

DR. COHEN: Yeah. I was just going to ask am I the only one hearing an echo.

DR. LIEBLER: It's Curt's phone. He's getting feedback from his computer. His phone's picking up the sound from his computer speaker. Then it's just recycling.

DR. KLAASSEN: I turned off my computer, and I'm listening on the telephone. Now, can you hear me?

DR. BERGFELD: Yes.

DR. KLAASSEN: And did the feedback disappear?

DR. BERGFELD: Yes.

DR. LIEBLER: Thank you, Curt.

DR. KLAASSEN: Okay. Finally.

DR. COHEN: So we thought leaving the malt in was just informational. We spent a lot of time on it as well, so we kept it in.

MS. BURNETT: Okay. Does the Belsito team agree with that, then?

DR. BELSITO: I don't know that we discussed the malt, Christina. Where is that in your introduction?

MS. BURNETT: We didn't, and that was my fault. I'm sorry. It's in the introduction. I guess that's the third or fourth paragraph down where it says "Many of the barley derived seed ingredients in the safety assessment (as well as the germinated and dry grain known as malt) may be consumed as food." So we mention it there and at the beginning of the toxicological studies section. It's not actually -- malt is not actually an ingredient in this report, so I don't know if that helps or hinders any understanding of what's going on.

DR. BELSITO: So I'm not an expert on brewing hard alcohol, so the malt obviously is used in production of some of them. What is the malt exactly? Is it seeds? Is it the leaves?

MS. BURNETT: It's a germinated seed, and then they dry it and crush it up. They use it for all sorts of stuff.

DR. BELSITO: So we can use it. Sure. I mean, it's part of the seed.

MS. BURNETT: Okay. We will leave it as is, then.

DR. BELSITO: Well, that's just my opinion. What about the other three members of my group?

DR. SNYDER: I agree.

DR. LIEBLER: I agree.

DR. SNYDER: I had in my notes to include it, so I'm fine.

MS. BURNETT: Okay. Thank you.

DR. BERGFELD: Do we think we're finished with barley, Dr. Belsito?

DR. BELSITO: I hope so.

DR. BERGFELD: I think after an hour we can move on. Dr. Cohen, you're up next. Diacetone alcohol.

MARCH 2022 PANEL MEETING – 4TH REVIEW/REVISED DRAFT TENTATIVE REPORT

Belsito's Team Meeting – March 7, 2022

DR. BELSITO: OK. OK. Our first of two botanicals to go- barley is up next. So at the December meeting, we issued an IDA, we wanted clarification of the plant parts used to make whole plant extract. Barley extract. The distichon and the vulgare. Method of manufacturing for the distichon extract and for the vulgare, extract composition and impurities for the extracts. 28 day dermal tox for the whole plant extract. And if positive additional data and dermal irritation sensitization for the whole leaf extract. So we did get some information. If I'm reading it correctly from the supplier when they talk about barley extract, it is seed extract, that's what they gave us back, right, Christina?

MS. BURNETT: Correct. But if Carol, if she's online, she might want to explain that data. It's actually under the way they use the way they used to file the ingredients, they did it more generically. So while it's a seed extract, it might not cover all of the Barley full plant ingredient names. Not sure I'm explaining that correctly, but...

DR. EISENMANN: Yeah. No, that's correct. I mean it, it's how they used to name ingredients without plant parts. So, this was leftover from then. Companies are really reluctant to change their names. So, so one supplier responded I didn't get response from all the suppliers. So, I don't know for sure if all the companies that are supplying.

DR. KLAASSEN: Except.

DR. EISENMANN: That the name without the plant part or grain or seed extracts. But I know one supplier is still selling a seed extract under the name without the plant part.

DR. LIEBLER: In other words, just calling it barley.

DR. EISENMANN: Right.

DR. LIEBLER: Exactly, yeah. So I thought about this too because it was a real sticking point for us last time, and the ones that are the non specified extracts are the ones with the high uses. And in the table the definition says whole plant. And based on the information just supplied to us and then some sort of logic, I think that whole plant probably is incorrect, and I think it's an inference that was drawn at some point it's incorrect. I mean, why in the world would you make an ingredient that required you to get the whole plant when what's really available in the marketplace is the grain, IE the seeds? I realize this isn't, you know, strict chain of custody for the, you know, for accounting for the manufacturing process, but it just seems to me logically much more correct that these extracts that aren't defined are not actually whole plant, but that are grain extracts.

DR. BELSITO: Well, it seems logical, but it's not the definition in the dictionary. I mean this is the problem.

DR. LIEBLER: Yeah. I mean, I think the definition is what's going to screw us over here because we...

DR. BELSITO: Well, that and what is reported to be used because the bulk of what's reported to be used as extract.

DR. LIEBLER: Right.

DR. BELSITO: Not seed extract.

DR. LIEBLER: Right. And that's what I'm saying, I think it's misclassified. I think it's most likely misclassified in the definition as whole plant. I think that's probably wrong.

DR. BELSITO: I'm pretty certain that it is misclassified, but how do we handle it? I mean, we can't. We can't say, OK, we just presume that the barley extract is really the seed extract.

DR. LIEBLER: So we say it's insufficient. Issue an insufficient report that they can't possibly respond to, because nobody who provides whole plant can give us the data. And so the most widely used ingredients are insufficient because of a naming convention problem. And then we're basically saying let God sort it out.

DR. EISENMANN: Well. I tell them all the time that you need- you should consider changing your name because the seed, if you add the word seed, you're into safe. So I don't know if that would...if they might start changing their names.

DR. BELSITO: Well, I guess I could have, Carol, because we can't rule on the extract, so it's going to.

DR. EISENMANN: I know, I know.

DR. BELSITO: So I mean, I think where we were before, I mean all of this seed materials are safe as used. And then the only question is about the leaf extract.

DR. SNYDER: But the seed and leaf are food, right? We found that we got that information didn't we?

DR. BELSITO: Yes.

MS. BURNETT: The sprouted grass is the food, yes. There's a debate on what a leaf and sprout is, how tall it grows before it's actually something else. I don't know.

DR. BELSITO: Hahaha...When does a boy become a man?

MS. BURNETT: Something like that. I mean, when I go to the grocery store and I see wheatgrass, it's usually like this tall, and that's what people use, you know, in their smoothies. They take it and grind it up. And it's usually like this tall, like your lawn. Whereas when you're harvesting it, the plant is this big, yellow dried out thing and it's got all sorts of stuff on the stalk, and it's got all sorts of leaves and stuff hanging off of it. So where the actual leaf is on that definition, I don't know.

DR. BELSITO: OK.

DR. LIEBLER: Well.

MS. BURNETT: I know previously in the wheat report there was an actual defined when it's this tall, it's considered to be like grass or sprout or whatever and then once it's beyond that height, that's a full plant or something.

DR. SNYDER: So do you, did you think we had enough composition and impurity data now, Dan?

DR. BELSITO: For which?

DR. LIEBLER: For the... Let's see.

DR. SNYDER: Looks like we have quite a bit for Ron.

DR. LIEBLER: We do for everything except we don't have it for the two major extracts, the distichon and the vulgare extracts because its parenthesis as an extract of the grain as opposed to the whole plant. Which again points to, I think the name confusion, I think the reality is that again that you know the widely used ingredient as an extract of the grain, not an extract of the whole plant. But so strictly speaking, we don't have sufficient composition, impurities for the whole plant. So that's still insufficient.

DR. BELSITO: Right.

DR. LIEBLER: And if the definition was corrected, then we're home free.

DR. BELSITO: So we don't have that information. So where are we here now with these? All of the seed ingredients are fine.

DR. LIEBLER:
Yep, and a leaf.

DR. BELSITO: And you're doing that based upon your belief that the leaf is grass, even though we're told the sprout is grass?

DR. LIEBLER:
Yeah. Food use.

DR. BELSITO: Pardon.

DR. LIEBLER:
Food use for the leaf.

DR. BELSITO: OK. Do we need sensitization and irritation for the grass?

DR. LIEBLER: For the leaf you mean?

DR. BELSITO: I thought we were assuming the grass was food now.

DR. LIEBLER: Yes.

DR. BELSITO: Right. So, we don't have sensitization or irritation.

DR. LIEBLER: We don't, OK. Then that's insufficient.

DR. SNYDER: Or. But it's a botanical.

DR. BELSITO: But it's not a botanical that contained sensitizers, so we can't get that when formulated to be non sensitizing to clear it. The grass also has some medicinal uses and the sprout you said is GRAS, Christina?

MS. BURNETT: I don't think it has that formal designation, no. It might be eaten, but I don't think - because it's not a food additive, it has that formal designation.

DR. LIEBLER: So.

DR. BELSITO: So is there?

DR. SNYDER: It's just known as the food, yeah?

MS. BURNETT: Right as a food use.

DR. BELSITO: So we don't sensitization for that.

DR. ANSELL: Yeah.

DR. LIEBLER: Right.

DR. BELSITO: Anything with the stem, flower, root is insufficient for composition or significantly different from the grain - 28 day dermal.

DR. LIEBLER: Right.

DR. BELSITO: And if it absorbs, tox endpoints. So the seed ingredients are all safe as used. The barle grass and barley sprout needs sensitization, and irritation and stem, flower, root insufficient for composition. Correct?

DR. SNYDER: Yes.

DR. LIEBLER: Yep.

DR. BELSITO: OK.

MS. BURNETT: So from the previous IDA, I'm eliminating the first two bullet points.

DR. LIEBLER: Which are...?

MS. BURNETT: Clarification on plant parts and method of manufacturing of the whole great whole plant extracts.

DR. BELSITO: I think we got as much as we can get, but it's.

MS. BURNETT: Alright, so go ahead and leave it, OK?

DR. LIEBLER: Don't leave it.

DR. BELSITO: Just say insufficient for composition. You can leave it there, sure.

DR. LIEBLER: Yep. Yep. That's still the main needs for these ingredients. There's still not, well...So we don't have the whole plant method of manufacture and composition impurities.

DR. BELSITO: But isn't this a tentative report now, right?

MS. BURNETT: And this is the second time it's tentative.

DR. SNYDER: Yes.

DR. BELSITO: This is a tentative final?

MS. BURNETT: They were. This is a revised tentative report. It went to the last meeting as a draft final. And then you guys put out a new insufficient data announcement.

DR. BELSITO: Right, right, it will be at next time it comes back to us, it'll be a tentative final.

MS. FIUME: It will issue as a revised tentative.

MS. BURNETT: Correct, correct.

DR. BELSITO: OK so...

MS. FIUME: No. It'll be a draft final the next time it comes back, it'll go out as a revised tentative and come back as a draft final.

DR. BELSITO: OK, so our conclusion is the seed ingredients are safe as used. The others are insufficient. And the grass and the sprout we need sensitization and irritation. Flower, root, stem we need composition, and if significantly different from the grain, 28 day dermal and if absorbs, other tox endpoints. Is that correct?

DR. SNYDER: Yes.

DR. BELSITO: OK. Christina, you're OK with that?

MS. BURNETT: Yes.

DR. BELSITO: OK, so come it's 3:30. Can we take a 5-minute break?

Cohen's Team Meeting – March 7, 2022

DR. COHEN: OK to move on to Barley?

DR. BERGFELD: Yeah.

DR. SLAGA: Yep.

DR. COHEN: So. It's a draft, tentative, draft, tentative?

MS. BURNETT: Yes.

DR. COHEN: Yeah, on 16 ingredients in December we issued an IDA. I'm looking for clarification of the plant parts that make the whole plant extracts for both distichon and vulgare, method of manufacturing for the extracts of both, composition and impurity, and 28 day dermal tox on the whole plant. And if positive, further data alternatively acceptable as a food would bypass that need. And dermal irritation and sensitization for the leaf extract. So we learned that the extracts were the grain right? Not the whole plant?

DR. BERGFELD: Would that be the seed?

MS. BURNETT: Well.

DR. BERGFELD: That would be the seed, the grain.

MS. BURNETT: Well. If Carol could speak to this they could be falling under old nomenclature rules. Carol, did you want to explain the data that we received?

DR. EISENMANN: Well, one company in the past and when ingredients were named, they were named without the plant part. And then when they started adding the plant part, some companies did not move their names, their trade name, materials over to the ingredients that have plant parts and they're still using the name without the plant part, unfortunately. It's very hard to get some companies to change names. So, whether the company that responded, is still making a making a grain extract or a seed extract and using the name that's now supposed to be for the whole plant extract. Now not all company unfortunately, not all companies will respond when I send out a request. So I don't know if that's the case. And whenever I tell like CIR SSC or other council committees, I tell them that the whole plant is has insufficient data, but you just may have a naming issue rather than we may just need to change the name and add seed and you have a safe ingredient, so it is being like, I wish I could say all of the ingredients that

under that name are made from what the definition says, but I can't confirm that. And there are no plans at this point to change names because of the reluctance of companies who changed their names.

DR. COHEN: Yeah, yeah. I was worried when I saw that because I thought for all this time we were using the word extract for the whole plant and then this came back is grain. But Carol, it sounds like you've sort of suggested that that may not be a universal adoption of the term extract. But I really thought about all the past ones we've done with the word extract, assessing it was the whole thing, pulled from its hair out of the earth and ground up. Ok, so...

DR. SHANK: I think we can say the seed ingredients are safe.

DR. BERGFELD: Right.

DR. SLAGA: Yeah.

DR. SHANK: And then leave the rest. That we've already had in the IDA.

DR. SLAGA: Yeah.

DR. COHEN: So.

DR. SLAGA: Fine with that. That's the easiest way to go with the seed being safe and the rest insufficient.

DR. COHEN: And is it insufficient for tox or you want more sensitization, irritation? Why? Let me put some perspective on it. There is Pub Med, many Pub Med publications on Barley grasses as food. There's lots of data on it being food and it's not just from Internet, Google searches, it's there in peer reviewed journals.

DR. SHANK: And barley grass is what?

DR. SLAGA: What is it? Yeah.

DR. BERGFELD: Is it the stem and the leaf?

DR. COHEN: Well, I would assume, I might assume it's at least the leaf.

MS. BURNETT: The sprouting grass is how I would characterize it.

DR. SLAGA: Sprouting grass right?

MS. BURNETT: Right.

DR. SLAGA: So yeah. That's why I will not return, but it would be this coming up from the...

MS. BURNETT: So it's very young, is about this tall, yeah.

DR. SLAGA: The seed...

DR. SHANK: Coming up from the seed.

DR. BERGFELD: So let's see.

DR. SLAGA: The sprout like. The grass that would be the grass, the first part to comes up?

DR. COHEN: Ah. Flower, leaf, stem, and roots. So where are we with clearing all of the seed ingredients?

DR. BERGFELD: Right.

DR. COHEN: Which leaves. The sprout extract. The stem.

DR. BERGFELD: Flower leaf.

DR. COHEN: And the sprout extract, were we going to not include, because if it's food... If we're going to say the sprout is food, do you feel we need more, more data on that?

DR. SHANK: No.

DR. SLAGA: No, that would be part of the seed then there we're talking, right?

DR. SHANK: I would put it yes.

DR. SLAGA: Yeah, put it in with the seed because it can sprout.

DR. COHEN: So you're considering the sprout a seedling?

DR. SLAGA: Right.

DR. COHEN: Part of the seed, but that has stem and leaf in it.

DR. SHANK: No, it doesn't. Not the sprout.

DR. SLAGA: Later on, Rosa does, but not. Not as a sprout.

DR. SHANK: No leaf.

DR. COHEN: I think when...

DR. SLAGA: It has potential in it to develop the rest of the plant.

DR. COHEN: But Barley grass, seemed to me when I went... when I was reading about it is, it's not just a sprout, it's a more mature component of this, right? I mean that would be barley sprouts, right?

DR. SHANK: OK So it's everything but the root.

DR. COHEN: I think that's why we need a food expert on here or a consultant. But I just wonder whether we're keeping out things that people are eating and we have enough data to conclude there probably OK.

DR. SLAGA: Well, cattle will eat all of it so...

DR. SHANK: Well, we asked for the information and nobody came back with anything.

DR. SLAGA: That's right.

DR. COHEN: Those are, those are straight facts.

DR. SLAGA: Yes.

DR. COHEN: Yeah. OK. Alright, insufficient on the rest.

DR. BERGFELD: Can we? OK, I've got that. Never mind. I've found it. I wanted to put a boilerplate in there, but it's in there, OK.

DR. COHEN: OK. Any other thoughts?

DR. SHANK: No. So where are we all the seed ingredients are safe and the rest are insufficient?

DR. COHEN: Well, I think you gave the green light to sprout.

DR. SHANK: OK, so the seed flour, the seed extract, the seed water and the sprout. Now my understanding was a sprout was a very early stage of germination.

DR. BERGFELD: That's what it says at the bottom and table two, yeah.

DR. COHEN: That's what I expected. And I guess if, that's if leaves are eaten, if leaves are eaten, it would clear leaf extract leaf juice? Leaf powder?

DR. SHANK: Yes.

MS. BURNETT: As a note on that, let me look at the insufficiency again. I don't believe we received the dermal irritation and sensitization data that was requested go with that.

DR. COHEN: I know.

MS. BURNETT: That's what's the missing component that I believe hangs up the leaf extract.

DR. SHANK: OK.

DR. COHEN: Right. And on the flip side is that there's another issue, which is we're treating vulgare and distichon separately when it comes to irritation and sensitization. Right. We were doing that. And so, when I look at that, we're not reading across the different products and so they're winding up in the same report. And they're being treated as two parallel, separate things, just because they're called barley or hordeum.

DR. BERGFELD: The genus of.

DR. COHEN: Right and so you know, I understand from one cultivar to the other, there's going to be differences, but there's going to be differences between the vulgare between cultivars. So why, why are we asking for irritation and sensitization for both of them? If we're putting them in the same report? Why are we not satisfied with distichon? We have HRIPT at 2.76%. And max use way below that. Right. So are we, are we always going to be doing this if we have different varieties in the same report? Are we going to just need parallel groups of sensitization and irritation data?

DR. SHANK: Well, we asked for data to allow us to see if how big a difference there is between cultivars, and nobody provided anything.

DR. SLAGA: Yeah.

DR. COHEN: But is it just for argument, right? If there were big differences in distichon from cultivar to cultivar, we would still clear it because we have HRIPT above max use. We were saying, OK, there's going to be differences here. But we have max use on a cultivar like, we don't even know what that might be. Right. But we're not willing to read across to vulgare.

DR. BERGFELD: I think the botanicals are different and the fact that they can have different chemical composition even though they may have overlaps.

DR. HELDRETH: Right when we have, when we have a botanical like this under one ingredient name and different cultivars, we're relying heavily on the conclusion being safe, safe with qualification, but as used as reported in this document, that's always part of the conclusion. And so we're saying or that you're saying that this ingredient is safe as used as reported here. So, your conclusion only pertains to whatever cultivar was presented here. If someone chooses to make another cultivar and use it, even in the exact same fashion, your conclusion doesn't

necessarily apply to their product. I mean we have those same issues with even discrete chemicals. You know someone may have different impurities and that may make it unsafe or insufficient.

DR. COHEN: Yeah. No, like.

DR. HELDRETH: But that, that's outside of the realm of what we can do. We can't. Can't hit all possibilities. So we have always had a caveat in our conclusion as “explained in this report”.

DR. COHEN: Yeah. No, I completely agree with that. It means...it's... we only can use the data we have and we can't predict new things that may evolve or a new strain that may be formed through a hybrid. But I did the question and I'll move on because if there's no further discussion about it, but if we looked at the vulgare cultivars, there's this big difference in the final compositions between the two vulgares. Right. So if we're OK with that and we're clearing distichon, which we don't have cultivars on, right? I don't think we do. Then why don't we allow vulgare and distichon to be discussed together because there's so much variety, there's so much variability even within the same species and genus. Why we even putting them in the same report if we're not willing to read across on that report? I guess I need answers.

DR. BERGFELD: Bart, you can answer that one.

DR. HELDRETH: Yeah, I mean. We played, we played with this grouping versus reader crossed and inference strategies. Unfortunately, it's a little bit of a, which comes first, chicken or the egg kind of situation. We have to group them together before we have gone out and searched all the data and received all the data submitted by industry. It would be great if we could have all that data that in front of us when we're deciding on what the group is going to be. But since we don't, we make our best educated guess on what a good grouping would be and then deal with the differences within one report. And so a lot of times we will have conclusions where you know these species are these plant parts or these cultivars are safe and the other ones have a different conclusion.

MS. BURNETT: I'd also like to note we kind of got hamstrung with the INCI naming. Barley actually falls under the distichon ingredients, it's not held in the title of the vulgare. So while vulgare is the more common barley species used, distichon is the one that actually has the barley name attached to it. In the INCI Dictionary, I should say.

DR. COHEN: So going forward, we still are happy putting them all together in the same report and then just asking for parallel sets of information for convenience sake, I suppose so people don't have to say holy cow, which barley are we buying this time for this face cream?

DR. SLAGA: Yep.

DR. COHEN: OK.

DR. EISENMANN: And the naming whether or not barley is included, they used to, again, it's timing of the name they've used to put him more routinely the common name, but now they're trying to move away from that. So it's not, it's not something intentional that this is barley and the other ones not barley. It's just the timing of when it was named.

DR. COHEN: Yeah, I was trying to group them together and be a bit more liberal with our conclusion because I thought it was reasonable to do that, but, I don't think the group shares that so. Don't be presenting this one. We will go with an IDA on everything that we had before, but seed and sprout ingredients are safe.

DR. SHANK: Yes.

DR. COHEN: It's going to be an interesting discussion, I think.

MS. BURNETT: So before we move away, the current draft discussion is sufficient. It's pretty...I think it mirrors what we had before.

DR. SLAGA: Right.

MS. BURNETT: OK.

DR. COHEN: Yeah. And you have the heavy metals in there.

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DR. BELSITO: OK. So, barley at the December meeting, we again issued an insufficient data announcement. We wanted clarification of the plant parts used to make the whole plant extracts. The whole plant extracts for *Hordeum Distichon* and *Hordeum Vulgare*. Which we basically got back are reports that they are extracts of the seed. We asked for method or manufacturing for *Hordeum Distichon* extract and *Vulgare* extract, composition and impurities on these extracts, and a 28 day dermal on the whole point. (indistinguishable)..we really didn't get any of that. We had a long discussion on this. I...we think industry is calling the extract of the seed just extract but unfortunately. Right. As defined in the dictionary, it's the extract of the whole plant and we (indistinguishable). So, we really can't get to clearing what is really the major ingredient family here, which is just the extract. Having said that, we feel that we can go ahead and say that all of the seed ingredients and the GRAS ingredients and the sprout ingredient are safe as used. Anything containing the stem, the flower, the root, or the whole plant, which we don't know what it is is insufficient for composition and if the composition is significantly different from the grain and the grass than a 28-day dermal and if absorbed, other toxicity endpoints may be needed and if significantly different, sensitization and irritation data would also be needed. So basically, we're going ahead. I believe this will be a tentative final. The seed ingredients, the grass, GRAS, and the sprouts are sufficient. The others, which include the extract which appears to be the major ingredient used, is unfortunately not supported at this point.

DR. BERGFELD: That's a motion, I gather.

DR. COHEN: Yeah. So, can I comment before a second?

DR. BERGFELD: Yeah, yeah, sure.

DR. BELSITO: Yep.

DR. COHEN: Yeah. It sounds like our conversations were very parallel. We came up with seed and sprout ingredients and insufficient for the flower, leaf and stem. Products when you say GRAS...are you talking about the leaf?

DR. BELSITO: (indistinguishable)

DR. LIEBLER: Yes.

DR. BELSITO: Yeah.

DR. COHEN: Because it's not meant, it's in the data profile, it's not described as GRAS, right? And unless I'm reading it wrong and it's you're clearing the grass because it is eaten?

DR. BELSITO: Yes. Yes.

DR. COHEN: And so could you define on the barley derived ingredient data profile just specifically? The ones that you're clearing and the ones that you're excluding, I know there there's 16 of them there. Maybe just talk about the ones you're excluding. So, we're on the same page, cause, we didn't use the word grass.

DR. BELSITO: OK. So, the ones we're excluding are the whole plant extract.

DR. COHEN: Yeah.

DR. BELSITO: *Distichon* and the *vulgare*, the juice, the powder, the root extracts. And the stem water.

DR. COHEN: Yeah.

DR. SHANK: So, what is the leaf? I mean the grass.

DR. BELSITO: The leaf?

DR. LIEBLER: I think the confusion stems in part from the non-cosmetic use section of the last paragraph where it says barley leaves also called barley grass “GRASS” have been described as developing functional food, so that's what Don's referring to is to leaves.

DR. SHANK: OK. Thank you.

DR. BELSITO: Right.

DR. COHEN: And we believe collectively that we have enough evidence that the leaves are food.

DR. BELSITO: Yes.

DR. COHEN: OK. Wow.

DR. BERGFELD: Do we have a reference on that?

DR. COHEN: Christina's got her hand up.

MS. BURNETT: I just wanted to clarify some of the other ingredients on the list. There's one that has flower and stem. I assumed that one's not safe.

DR. BERGFELD: You're...

DR. BELSITO: Correct.

MS. BURNETT: Or insufficient. I'm sorry, insufficient.

DR. SHANK: Insufficient.

DR. COHEN: Yeah, not cleared.

MS. BURNETT: Yeah. And the same with the leaf slash stem powder.

DR. BELSITO: Yeah.

MS. BURNETT: OK. I think we included in the non-cosmetic use section at least one or two references that describe it as food or I'm. I'm looking. I'm sorry I thought we had...

DR. COHEN: Yeah, we got a bit caught up on the leaves as food.

DR. LIEBLER: This is this is ine where it's just referenced. 62 is cited, Christina, in the middle of the third paragraph of non cosmetic and it says has been described as a developing functional food in powder form with novel preventative drug potential. I haven't seen the paper, but I can imagine that that's an assertion made in the introduction and the paper goes on to be about the...

MS. BURNETT: Yeah.

DR. LIEBLER: The effects of this stuff. So, I mean this is on the low end of the evidence scale for food use in, in my opinion. So, this is one of those ones where it's kind of borderline evidence of food use. Correct.

DR. COHEN: Right. We didn't clear it because we didn't seem to have the food evidence that we had with Portulaca.

DR. BELSITO: I'm fine not including it. I mean, I don't even think there are any cosmetic uses. (indistinguishable)

DR. COHEN: Ah.

DR. BELSITO: I'm just going with all the seed ingredients. Let me.

DR. COHEN: And sprout.

DR. BELSITO: Thanks.

DR. LIEBLER: Yep.

DR. COHEN: We cleared seed and sprout.

DR. BELSITO: Just trying to get them to the table.

DR. LIEBLER: I have no problem with that.

DR. BELSITO: Yeah, I mean, they were never (indistinguishable). There are some uses for the leaf extract and leaf juice. But I mean, I'm fine with seed and sprout. I mean it is very... it's not very strong evidence for food and any of the leaf...

DR. BERGFELD: I have a question. There is someone in the audience with a question.

DR. BELSITO: Yeah.

DR. BERGFELD: And it went down. I had proposed yesterday that perhaps we needed some kind of internal document in what we considered food and GRAS. Because this has been a continued discussion through this group of ingredients.

DR. BELSITO: Yeah, but I think it's sort of hard to, I mean, it's almost like if you take it case by case and look at what the evidence is.

DR. COHEN: We've also...

DR. BERGFELD: Well, I think that's true. What we do know is something we knew something about GRAS, food additive GRAS and food additives and then case by case, we could take it. But I suspect we would need references to support whatever we called a food. Anyhow, I'd like to pose that question to Bart. Maybe he could develop some basic sort of document. OK, we have a continued our discussion here with barley and do we have a motion? Seconded.

DR. BELSITO: Seed and sprout ingredients are safe, all the others are insufficient (indistinguishable).

DR. BERGFELD: We described what we want to appear in the discussion, the insufficiency list, of course. Is there anything else in particular? The metals, probably heavy metals disclaimer...

DR. BELSITO: I mean usual botanical. There are no sensitizers, so we don't need the botanical sensitizer boilerplate.

DR. BERGFELD: Yeah. In.

DR. BELSITO: But the, you know, heavy metals, pesticides...

DR. LIEBLER: So Janet, Janet Zang has her hand back up.

DR. BERGFELD: Anything else? OK. Janet.

DR. ZANG: Hi. This is Janet Zang from FDA. Can you guys hear me OK?

DR. BERGFELD: Yeah. Uh-huh.

DR. ZANG: Great. I, you know basically originally, I had a question similar to what Wilma?

DR. SLAGA: It's...

DR. ZANG: Dr. Bergfeld...I wanted to stress that GRAS with the meaning of generally recognized as safe is a very specific meaning. In terms of food additives, I think this point was brought up in the Belsito group yesterday and I would very much welcome the proposal by Dr. Bergfeld with CIR develop some general guidance or some...? Had some general discussion about the definition of GRAS and food use because they are different. That's what I'm trying to say here. Thank you.

DR. BERGFELD: Thank you.

DR. SNYDER: I think our premise is that a food is eaten. GRAS is a direct additive that has been approved, but we also have indirect food additives like where you had with the polymer. So, I think those to me...that's how the three that I look at it as one is a direct food additive approved GRAS, one is an indirect food additive, usually a film or something like that. It comes in contact with food and the other one is a food because it's eaten.

DR. BERGFELD: OK.

DR. ZANG: That's more like...I would say that that's not entirely correct. Per the US regulation, GRAS is a kind of food ingredients, but they're not necessarily go to the regulation because GRAS is voluntary.

DR. BELSITO: Yes.

DR. ZANG: Voluntary. Has a voluntary mechanism have there are some self-GRAS, so I would very much like CIR to have a further check on the regulation yeah.

DR. BERGFELD: Thanks. Alright, Thomas, are you there?

MR. GREMILLION: Yeah, I just wanted a second at that point. That grand. There's self-determination with GRAS and a lot of the consumer groups. But my own, you know, secret GRAS determinations and it's not, we wouldn't call it an approval. So yeah, just to echo that point.

DR. BERGFELD: Is that another category secret GRAS?

MR. GREMILLION: I mean it's a self-determination and there's no obligation after the self determination to disclose that the determination was made. So, some of these food ingredients can be GRAS.

MS. KOWCZ: Yeah.

MR. GREMILLION: But as determined by them by their manufacturer and undisclosed to FDA or anybody else.

DR. BERGFELD: Well, I think we can take that into consideration. There are going to be multiple categories that we might start to develop. So, we understand what they're talking about when it's mentioned.

DR. SHANK: GRAS is defined by FDA. Period.

DR. BERGFELD: Yeah, I mean that one, Secret.

MR. GREMILLION: So.

DR. SHANK: That's it. It's not an arguable point.

DR. BERGFELD: Right.

MR. GREMILLION: So.

DR. BERGFELD: No, no, no. But just to define it along with the other foods.

DR. SHANK: OK.

MR. GREMILLION: So it may be Janet can elaborate on kind of the...Yeah. About the different GRAS substances or categorizes but as for like in? New determinations can be made every day. You know it's a...

DR. BERGFELD: OK. Well, we'll have Bart get in the order, Janet.

DR. ZANG: There is still GRAS inventory list on the FDA website.

DR. BERGFELD: OK.

DR. ZANG: OK.

DR. BERGFELD: Great, thank you. Alright, I we were...

DR. BELSITO: Alexandra.

DR. LIEBLER: Alex has a comment.

DR. BERGFELD: OK. Yeah.

MS. KOWCZ: Yeah, I just have a quick comment to Janet possibly and maybe Bart. If this is even coming up as a subcategory, I've never heard of secret GRAS, to be honest, in my entire almost 40 years of doing cosmetics formulation and being in the industry, I would very much like a presentation possibly from the FDA to describe this. I'm just...

DR. BERGFELD: Well, they're not approving them.

DR. ZANG: I have not heard a definition of secret GRAS and...

MS. KOWCZ: Right OK, but if there is such a thing?

DR. ZANG: Yeah, and there are definitions on FDA's website in terms of food ingredients, as I'm willing to share from website.

MS. KOWCZ: Right.

DR. BERGFELD: OK.

MS. KOWCZ: But yeah, that if there is any event.

MR. GREMILLION: Well, let...

DR. ZANG: Yeah, to get more understanding.

MS. KOWCZ: Yeah. But Janet, we just want to make sure that everyone is understanding, and everyone is working from the same platform and from the, you know, (indistinguishable). I've always understood GRAS to be generally recognized as safe and effective. And if they aren't...

DR. BERGFELD: OK.

DR. ZANG: That's correct.

DR. SHANK: For food additives.

MS. KOWCZ: (indistinguishable) also for you know, for any material on the OTC category, whatever. So, I think Janet, if we can also just make sure that everyone here on this panel and even the people that are part of this could really understand your definition because I'm a bit concerned that Thomas is saying that there's secret GRAS and things like that if which I've never really heard of. So, if we can get some of those, you know references that would be wonderful Janet and very much...

MR. GREMILLION: Yeah.

MS. KOWCZ: Appreciated by everyone here. Thank you.

DR. ZANG: I'm not, I'm afraid I don't have reference for secret GRAS, but I can get you the federal guidance? Yeah, the FDA definition of GRAS, of course.

MS. KOWCZ: No, but for GRAS. Correct.

DR. BERGFELD: Thank you.

MS. KOWCZ: And of course, Bart can always reach out to Linda, and we can talk to her, too. Thank you.

DR. BERGFELD: Thank you.

MR. GREMILLION: Good.

DR. BERGFELD: Thomas. Something more you're saying?

MR. GREMILLION: Yeah, I just wanted to clarify that you know that there are substances that that, you know, a producer can evaluate themselves and self-determine to be GRAS and there's no obligation to make that self-determination public. You can. Yeah, you can.

DR. BERGFELD: Official.

DR. BELSITO: (indistinguishable) unless it's not GRAS, they can determine that it is safe for consumption, but it's not GRAS status.

MS. KOWCZ: Right.

DR. SNYDER: Yeah, I've never. I've never heard that before.

DR. SHANK: Correct.

MS. KOWCZ: We have never heard that before, Thomas. Never.

MR. GREMILLION: I'm happy to follow up with them.

DR. BERGFELD: Thank you. Please help.

MS. KOWCZ: Yeah, maybe follow up. That's a good idea.

DR. LIEBLER: So.

DR. BERGFELD: But still.

MR. GREMILLION: Alright, thanks.

DR. LIEBLER: Wilma, can I make a suggestion here? Because I think we've kind of drifted from the issue for us, for this panel, is that we just need some greater degree of standardization or assertion of what are...

DR. BERGFELD: (indistinguishable)

DR. LIEBLER: Guidelines for accepting that a chemical has a food use or that there's some substance has a food use, and I think the, you know, GRAS classification where whatever the legitimacy of it is one of the things we take into consideration. We take into consideration literature, we take into consideration a body of ethnopharmacology in some cases, etc. I think this doesn't need to be another like inhalation resource.

DR. SLAGA: Right.

Dr. Dan Liebler -
Document, but I think, crisply written one pager would do a so.

DR. SLAGA: No.

DR. LIEBLER: Something like that might be possible. Bart, that's my \$0.02 worth. I just like to see some, maybe even bulleted listing of the types of evidence that the panel considers when asking whether or not something has food uses and they're therefore would guide our determination of systemic tox risk.

DR. COHEN: I agree with that Dan, I think one issue is if we have an ad hoc consultant, there are many universities that have a whole school on dietary science where we could just get an opinion that this is food. Right, that someone who specializes in this can review the data out there and say, yeah, people eat this, and it seems to be safe.

DR. BERGFELD: I think that we can assign this first to Bart to get us a working document. Then we can move from there. So I'm going to close this discussion and I'm going to call for the vote, which I don't think I did.

DR. BELSITO: I just.

DR. BERGFELD: All those in favor of the conclusion that was made on barley, yes, barley with the list of insufficient data on some of the barley plant part. Any opposed? Abstaining? It's approved, so moving on. Dr Cohen to Rosa Centifolia.

DR. BELSITO: Just before we move on, Wilma, I'm I just want to echo something that Carol mentioned yesterday and just point out to industry that the vast majority of barley ingredients that they say they used are currently the data is insufficient and we strongly suspect that they're using seed extract and not whole plant extract and they should be much more careful in what they report.

DR. COHEN: OK.

DR. BERGFELD: Thanks. Thank you. I think that some of it is due to the dictionary and some of the new additions and definitions. So, we'd have to assign that also to Bart to rally for our cause of getting this clarified as well. OK, let's go on. Bart has something to say?

DR. HELDRETH: Yeah. I just wanted to say, you know, I've had the opportunity to work a little bit with the nomenclature committee that's behind the dictionary and part of the reluctance from members of industry to make those name changes to be more specific there because of international standards. For instance, for many, many years the Chinese FDA had had a situation at hand where only those ingredients named in a much, much older version of the dictionary was allowed to be used as ingredients in China. And so, if you came through and tried to promote a product in China using one of the newer, more specific names it would be unallowed. So, I think that a big part of their reluctance there to make those changes. Not it's not an intentional deception. They're making the change where they can, but we're not always going to see a quick migration to those more specific names. Much to my own personal dismay about it. But I do think that the dictionary folks can do something to the change. The monographs that the definition basically of those dictionary names so that it's more obvious to the panel and other readers that this may be the whole plant. This may be the seed depending on how it's used.

DR. BERGFELD: OK, I think that will clarify some things and our frustration.

Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Status: Draft Final Report for Panel Review
Release Date: May 23, 2022
Panel Meeting Date: June 16-17, 2022

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.; Allan E. Rettie, Ph.D.; David Ross, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; Paul W. Snyder, D.V.M., Ph.D.; Susan C. Tilton, Ph.D. Previous Panel member involved in this assessment: Lisa A. Peterson, 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 5 barley-ingredients (i.e., the seed- and sprout-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 11 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 previously 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 and sprout 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 the Panel typically evaluates, is provided on the CIR website (<https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites>; <https://www.cir-safety.org/supplementaldoc/cir-report-format-outline>). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics and without abbreviations. When referring to the plant from which these ingredients are derived, the standard scientific practice of using italics will be followed (i.e., *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.

Another supplier has reported on *Hordeum Distichon* (Barley) Extract as an extract of the grain.¹⁸ The barley grain is extracted with specified eluent(s) under appropriate temperature conditions, to yield a concentrate. Typical eluents include water, butylene glycol, *Carthamus tinctorius* (safflower) seed oil, glycerin, and propylene glycol. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient.

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

Barley flour is milled from pearled, blocked or hull-less barley.¹⁹ 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 Extract

A supplier has reported on *Hordeum Vulgare* Extract as an extract of the grain.²⁰ The barley grain is extracted with specified eluent(s) under appropriate temperature conditions, to yield a concentrate. Typical eluents include water, butylene glycol, *Carthamus tinctorius* (safflower) seed oil, glycerin, and propylene glycol. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient.

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.²¹ 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.²²

Another supplier has reported that Hordeum Vulgare Seed Extract is produced by harvesting hydroponically cultivated barley seeds, then drying and milling them.²³ 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.²⁴ 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).²⁵⁻²⁷ 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.²⁸ Table 3 describes the phenolic composition of three different parts of two different barley cultivars.²⁹ 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.^{9,26} Phytochemicals in barley grain include phenolic acid, flavonoids (flavanols, anthocyanins, proanthocyanidins), lignans, tocopherols, phytosterols, and folates.³⁰

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 fungi 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*.^{10,31,32} 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.³³

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 (EU) Cosmetic Regulations were below threshold levels for this concentrate.

Another supplier has reported that a concentrate of Hordeum Distichon (Barley) Extract (as an extract of the grain) in an alcohol base also had no detectable heavy metals or residual pesticides.¹⁸ The 26 fragrance allergens defined by the EU were also reported to be below threshold levels.

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%.³⁴ 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.³⁵

Hordeum Distichon (Barley) Seed Flour

Acetone extracts of *Hordeum distichon* grains contain 5-*n*-alkylresorcinols.²⁵ 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 Extract

A supplier has reported that a concentrate of *Hordeum Vulgare* Extract (as an extract of the grain) in an alcohol base had no detectable heavy metals or residual pesticides.²⁰

Hordeum Vulgare Juice

Phytochemical analysis of barley grass juice (15 d post-germination) was used to determine the presence of flavonoids, saponins, and terpenoids.³⁶ The total phenolic and flavonoid content was 225.33 mg gallic acid equivalents (GAE)/g and 203 mg quercetin equivalents/g of extract, respectively.

Hordeum Vulgare Seed Extract

Constituents of a water extract of *Hordeum vulgare* seeds included phenolics, flavonoids, anthocyanins, flavonols, tannins, triterpenoids, and vitamin C.³⁷ 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.³⁸ 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.³⁹ 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.⁴⁰ 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.⁴¹

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.⁴²

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.⁴³ 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.⁴⁴ 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.⁴⁵ 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.⁴⁶ 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, and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and,

therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety. Therefore, airbrush application of cosmetic products is not assessed by the Panel.

According to 2022 VCRP survey data, *Hordeum Vulgare* Extract has the most reported uses in cosmetic products, with a total of 174 formulations; the majority of the uses are in leave-on makeup preparations and skin care products (Table 5).⁴⁷ *Hordeum Vulgare* Seed Extract has the second greatest reported number of uses in this safety assessment with 33 formulations; the majority of the uses are in leave-on skin care products. *Hordeum Distichon* (Barley) Extract has 31 reported uses; the majority of the uses are also in leave-on skin care products. The remaining 4 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.⁴⁸ 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.⁴⁹ No concentrations of use were reported for any of the other barley-derived ingredients in this report. The 9 ingredients not in use, according to the VCRP and industry survey, are listed in Table 6.⁴⁷⁻⁴⁹

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.^{48,49} 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.⁴⁸ In practice, as stated in the Panel's respiratory exposure resource document (<https://www.cir-safety.org/cir-findings>), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

Although products containing some of these ingredients may be marketed for use with airbrush delivery systems, this information is not available from the VCRP or the Council survey. Without information regarding the frequency and concentrations of use of these ingredients (and without consumer habits and practices data or particle size data related to this use technology), the data are insufficient to evaluate the exposure resulting from cosmetics applied via airbrush delivery systems.

The barley-derived ingredients described in this report are not restricted from use in any way under the rules governing cosmetic products in the EU.⁵⁰

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.⁵¹ 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.^{37,38,52,53} Barley seed flour applied topically has been studied for therapeutic benefits in infants with jaundice.⁵⁴ Barley leaves, also called barley grass, have been described as a developing functional food in powder form, with novel preventative drug potential.⁵⁵ Young barley grass water and juice extracts have been studied for obesity inhibition³⁶ and chemopreventative potential in human colon and lung cancer cell lines,^{56,57} while young green *Hordeum vulgare* leaves have been studied for anti-stress properties that could be beneficial in treating psychiatric disorders such as depression.⁵⁸ Barley sprout "essence" and extract has been studied for its effects on blood cholesterol and treatment for chronic alcohol-induced liver injury.^{12,59-61}

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 sprout ingredients in this safety assessment (as well as the germinated and dried grain known as malt) 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 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

In Vitro

Hordeum Vulgare Leaf Extract

A bacterial reverse mutation assay was performed on the polysaccharide fraction of young *Hordeum vulgare* leaves at up to 5000 µg/plate.⁶² Dried barley leaves underwent enzyme digestion and extraction to obtain the final test material. *Salmonella typhimurium* strains TA98, TA100, TA1535, an TA1537 and *Escherichia coli* strain WP2uvrA were utilized, and the assay was performed with and without S9 metabolic activation in accordance with Organization for Economic Co-Operation and Development (OECD) test guideline (TG) 471. No cytotoxicity or mutagenicity was observed in the test material, with or without metabolic activation. Positive controls yielded expected results. It was concluded that the polysaccharide fraction of young *Hordeum vulgare* leaves did not induce reverse mutations.

The same research group also performed a chromosomal aberration assay on the same test material at up to 1000 µg/ml, in accordance with OECD TG 473.⁶² The assay utilized Chinese hamster lung fibroblast (CHL/IU) cells and was performed with and without S9 metabolic activation. The cells were treated with the test material for 6 or 24 h, and structural and numerical aberrations were observed after Giemsa staining. The frequency of structural abnormalities in the test material and negative controls was found to be 0%. The frequency of numerical abnormalities did not demonstrate a significant difference from the negative controls. The positive controls yielded expected results. It was concluded that the polysaccharide fraction of young *Hordeum vulgare* leaves did not cause chromosomal abnormalities.

No other 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).^{63,64} A mascara product containing 0.3% Hordeum Distichon (Barley) Extract was determined to not be sensitizing in a human repeated insult patch test (HRIPT; n = 111), but low-level (+) reactions were observed in the induction and challenge phases.⁶⁵ No dermal sensitization was observed with a lotion containing 1.8% Hordeum Distichon (Barley) Extract in a HRIPT (n = 102); however a slight potential for dermal irritation was noted.⁶⁶ Hordeum Distichon (Barley) Extract also was not irritating or sensitizing in an eye cream at 1.8% (n = 54);⁶⁷ 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.⁶⁸ 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.⁶⁹⁻⁷²

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.⁷³ Approximately a quarter of the subjects had self-perceived sensitive eyes, and more than half of the

panel (47) were contact lens wearers. Subjects were instructed to apply the mascara twice daily for 4 wk. An ophthalmologist conducted slit lamp examinations at the baseline, at the 2-wk interim, and final visits. Visual acuity was measured at the initial and final visits. Questionnaires seeking subject-perceived effects were completed by the subjects at the end of each 2-wk use period. No visible clinical irritation was observed related to the use of the test material and none of the subjects reported perceived discomfort or irritation during the study period.

Hordeum Vulgare Extract

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

Case Reports

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

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

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

OCCUPATIONAL EXPOSURES

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

EPIDEMIOLOGY OF IMMUNE-MEDIATED GLUTEN AND BARLEY REACTIONS

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

SUMMARY

Hordeum distichon and *Hordeum vulgare* are two species of barley, an annual grass, that is cultivated as a cereal grain. Most of the 16 barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents. The Panel has previously 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 2022 VCRP survey data, *Hordeum Vulgare* Extract has the most reported uses in cosmetic products, with a total of 174 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 33 formulations; the majority of the uses are in leave-on skin care products. *Hordeum Distichon* (Barley) Extract has 31 reported uses; the majority of the uses are also in leave-on skin care products. The remaining 4 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 9 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 parts 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 and sprouts, 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.

The polysaccharide fraction of young *Hordeum vulgare* leaves was not mutagenic in a bacterial reverse mutation assay at up to 5000 µg/plate, with or without metabolic activation. The same test preparation did not induce chromosomal abnormalities, with or without metabolic activation, when tested at up to 1000 µg/ml in CHL/IU cells.

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, or carcinogenicity 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 5 ingredients, i.e., those derived from barley seeds and sprouts, as reportedly used in cosmetics. The Panel noted that the barley seed- and sprout-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 and sprouts of barley are commonly consumed as food, other barley plant parts are not widely consumed as food or have no designation as generally recognized as safe (GRAS) as food ingredients or additives, and safety test data are lacking. Thus, the Panel also concluded that data are insufficient for determining the safety for the non-seed and non-sprout ingredients. The additional data needed to determine safety of the remaining ingredients as used in cosmetics are:

- Explanation of the plant parts used to make the whole plant extracts Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Method of manufacturing for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- Composition and impurities data for Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
- 28-day dermal toxicity data on the whole plant extract Hordeum Distichon (Barley) Extract and Hordeum Vulgare Extract
 - If positive, additional data, such as developmental and reproductive toxicity and genotoxicity data, may be needed
 - Alternatively, acceptable evidence of safe use as food for the ingredients derived from the flower, leaf, stem, and root
- Dermal irritation and sensitization data for Hordeum Leaf Extract, or other leaf ingredients

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, **the majority** of the droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or **tracheobronchial** regions of the respiratory tract present no toxicological concerns **based on the chemical and biological properties** of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which the ingredients are used **(or expected to be used) in potentially inhaled products**, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. **As indicated in the respiratory exposure resource document and in the Cosmetic Use section of this report, airbrush application of cosmetic products in not assessed by the Panel.** 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 5 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 Water*
Hordeum Vulgare Seed Extract	Hordeum Vulgare Sprout Extract*
Hordeum Vulgare Seed Flour	

**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 11 barley-derived ingredients are safe under the intended conditions of use in cosmetic formulations:

Hordeum Distichon (Barley) Extract	Hordeum Vulgare Leaf Powder**
Hordeum Vulgare Extract	Hordeum Vulgare Leaf/Stem Powder**
Hordeum Vulgare Flower/Leaf/Stem Juice**	Hordeum Vulgare Powder**
Hordeum Vulgare Juice**	Hordeum Vulgare Root Extract
Hordeum Vulgare Leaf Extract	Hordeum Vulgare Stem Water**
Hordeum Vulgare Leaf Juice	

***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.²⁹

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

NR = Not reported.

Table 4. Composition of barley-derived ingredients

Constituent	Barley Seed Flour (generic) ^{34,35}	Hordeum Distichon (Barley) Seed Flour ²⁵	Hordeum Vulgare Leaf Juice ³⁶	Hordeum Vulgare Seed Extract ³⁷⁻³⁹	Hordeum Vulgare Seed Flour ⁴³	Hordeum Vulgare Sprout Extract ^{12,45,46}
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.

DM = dry material

GAE = gallic acid equivalents

Table 5. Frequency (2022)⁴⁷ and concentration (2018;⁴⁸ 2020⁴⁹) 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 Leaf Juice	
Totals[†]	31	0.005-1.8	174	0.000015-1.5	4	NR	2	NR
<i>Duration of Use</i>								
Leave-On	21	0.005-1.8	164	0.000015-1.5	4	NR	2	NR
Rinse Off	10	0.1	10	0.0015-0.15	NR	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure Type</i>								
Eye Area	4	0.005-0.3	7	0.005-0.075	1	NR	NR	NR
Incidental Ingestion	NR	NR	17	0.15	NR	NR	NR	NR
Incidental Inhalation-Spray	7 ^a ; 5 ^b	NR	3; 90 ^a ; 28 ^b	0.03; 0.03-0.038 ^a ; 0.03 ^b	3 ^b	NR	2 ^b	NR
Incidental Inhalation-Powder	5 ^b	0.005 ^c	1; 28 ^b ; 2 ^c	0.015; 0.03 ^b ; 0.001-1.5 ^c	3 ^b	NR	2 ^b	NR
Dermal Contact	19	0.005-1.8	151	0.000015-1.5	4	NR	2	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	12	NR	6	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	19	0.15	NR	NR	NR	NR
Baby Products	NR	NR	2	NR	NR	NR	NR	NR
<i>Hordeum Vulgare Root Extract</i>								
Totals[†]	1	NR	33	NR	2	NR	NR	NR
<i>Duration of Use</i>								
Leave-On	1	NR	30	NR	1	NR	NR	NR
Rinse Off	NR	NR	3	NR	1	NR	NR	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
<i>Exposure Type</i>								
Eye Area	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	12; 6 ^a ; 10 ^b	NR	NR	NR	NR	NR
Incidental Inhalation-Powder	NR	NR	10 ^b	NR	NR	NR	NR	NR
Dermal Contact	1	NR	33	NR	2	NR	NR	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	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	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	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.⁴⁷⁻⁴⁹

Hordeum Distichon (Barley) Seed Flour
 Hordeum Vulgare Flower/Leaf/Stem Juice
 Hordeum Vulgare Juice
 Hordeum Vulgare Leaf Powder
 Hordeum Vulgare Leaf/Stem Powder
 Hordeum Vulgare Powder
 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	⁶⁴
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	⁶³
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	⁶⁵
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	⁶⁶
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	⁶⁷

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	⁶⁸
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	⁷¹
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	⁷²
Pressed powder containing 0.005% Hordeum Vulgare Extract	Amount applied not reported; however, patches were moistened with several drops of water to ensure adherence of test material	107 subjects	HRIPT conducted in a similar manner as described above; semi-occlusive patches	Not a dermal irritant or sensitizer	⁶⁹
Skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract	Amount applied not reported	50 subjects	HRIPT conducted in a similar manner as described above; occlusive patches	Not a dermal irritant or sensitizer; no adverse reactions were induced	⁷⁰

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2022 FDA VCRP Raw Data

HORDEUM DISTICHON (BARLEY) EXTRACT	03D	Eye Lotion	4
HORDEUM DISTICHON (BARLEY) EXTRACT	05A	Hair Conditioner	5
HORDEUM DISTICHON (BARLEY) EXTRACT	05F	Shampoos (non-coloring)	3
HORDEUM DISTICHON (BARLEY) EXTRACT	05G	Tonics, Dressings, and Other Hair Grooming Aids	2
HORDEUM DISTICHON (BARLEY) EXTRACT	05I	Other Hair Preparations	2
HORDEUM DISTICHON (BARLEY) EXTRACT	07H	Makeup Fixatives	1
HORDEUM DISTICHON (BARLEY) EXTRACT	11E	Shaving Cream	1
HORDEUM DISTICHON (BARLEY) EXTRACT	12A	Cleansing	1
HORDEUM DISTICHON (BARLEY) EXTRACT	12C	Face and Neck (exc shave)	5
HORDEUM DISTICHON (BARLEY) EXTRACT	12F	Moisturizing	2
HORDEUM DISTICHON (BARLEY) EXTRACT	12I	Skin Fresheners	2
HORDEUM DISTICHON (BARLEY) EXTRACT	12J	Other Skin Care Preps	2
HORDEUM DISTICHON (BARLEY) EXTRACT	13C	Other Suntan Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	01B	Baby Lotions, Oils, Powders, and Creams	2
HORDEUM VULGARE (BARLEY) EXTRACT	03D	Eye Lotion	5
HORDEUM VULGARE (BARLEY) EXTRACT	03G	Other Eye Makeup Preparations	2
HORDEUM VULGARE (BARLEY) EXTRACT	04E	Other Fragrance Preparation	3
HORDEUM VULGARE (BARLEY) EXTRACT	05A	Hair Conditioner	1
HORDEUM VULGARE (BARLEY) EXTRACT	05E	Rinses (non-coloring)	1
HORDEUM VULGARE (BARLEY) EXTRACT	05F	Shampoos (non-coloring)	3
HORDEUM VULGARE (BARLEY) EXTRACT	05I	Other Hair Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	07A	Blushers (all types)	2
HORDEUM VULGARE (BARLEY) EXTRACT	07B	Face Powders	1
HORDEUM VULGARE (BARLEY) EXTRACT	07C	Foundations	2
HORDEUM VULGARE (BARLEY) EXTRACT	07E	Lipstick	17
HORDEUM VULGARE (BARLEY) EXTRACT	07F	Makeup Bases	4
HORDEUM VULGARE (BARLEY) EXTRACT	07I	Other Makeup Preparations	3
HORDEUM VULGARE (BARLEY) EXTRACT	10A	Bath Soaps and Detergents	2
HORDEUM VULGARE (BARLEY) EXTRACT	12A	Cleansing	2
HORDEUM VULGARE (BARLEY) EXTRACT	12C	Face and Neck (exc shave)	23
HORDEUM VULGARE (BARLEY) EXTRACT	12D	Body and Hand (exc shave)	5
HORDEUM VULGARE (BARLEY) EXTRACT	12F	Moisturizing	80
HORDEUM VULGARE (BARLEY) EXTRACT	12G	Night	10
HORDEUM VULGARE (BARLEY) EXTRACT	12H	Paste Masks (mud packs)	1
HORDEUM VULGARE (BARLEY) EXTRACT	12J	Other Skin Care Preps	4
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	03D	Eye Lotion	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	12C	Face and Neck (exc shave)	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	12D	Body and Hand (exc shave)	2

HORDEUM VULGARE (BARLEY) LEAF JUICE	12C	Face and Neck (exc shave)	2
HORDEUM VULGARE (BARLEY) ROOT EXTRACT	12J	Other Skin Care Preps	1
HORDEUM VULGARE (BARLEY) SEED EXTRACT	04E	Other Fragrance Preparation	12
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12A	Cleansing	3
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12C	Face and Neck (exc shave)	10
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12F	Moisturizing	5
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12I	Skin Fresheners	1
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12J	Other Skin Care Preps	2
HORDEUM VULGARE (BARLEY) SEED FLOUR	12J	Other Skin Care Preps	1
BARLEY FLOUR	12H	Paste Masks (mud packs)	1