Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	November 13, 2020
Panel Meeting Date:	December 7-8, 2020

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

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Cosmetic Ingredient Review

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Memorandum

To: Expert Panel for Cosmetic Ingredient Safety Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: November 13, 2020
Subject: Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Report of the Safety Assessment of Barley-Derived Ingredients as Used in Cosmetics. (It is identified as *barley122020rep* in the pdf document.) The Notice to Proceed (NTP) without the preparation of a Scientific Literature Review (SLR) of these 16 botanical ingredients was issued by CIR on August 5, 2020. These ingredients 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 Council provided concentration of use survey data (*barley122020data1* and *barley1220202data 7*), method of manufacturing, composition and impurities, and HRIPT data on Hordeum Vulgare Seed Extract (*barley122020data2; barley122020data5*), method of manufacturing and impurities on Hordeum Distichon (Barley) Extract (*barley122020data3*), method of manufacturing on Hordeum Vulgare Seed Water (*barley122020data4*), and ocular irritation and HRIPT data on Hordeum Vulgare Extract (*barley122020data6*). No comments on the NTP were received from the Council.

According to 2020 VCRP survey data (*barley122020fda*), Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 383 formulations; the majority of the uses are in leave-on skin care products. Hordeum Distichon (Barley) Extract has the second greatest reported number of uses in this safety assessment with 91 formulations; the majority of the uses are also in leave-on skin care products. The other 2 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 other 2 in-use barley-derived ingredients in this report. There are 12 ingredients not reported to be in use, according to the VCRP and industry surveys.

Additional supporting documents for this report package include a flow chart (*barley122020flow*), report history (*barley122020hist*), a search strategy (*barley122020strat*), and a data profile (*barley122020prof*).

If no further data are needed to reach a conclusion of safety, the Panel should formulate a Discussion and issue a Tentative Report. However, if additional data are required, the Panel should be prepared to identify those needs and issue an Insufficient Data Announcement.

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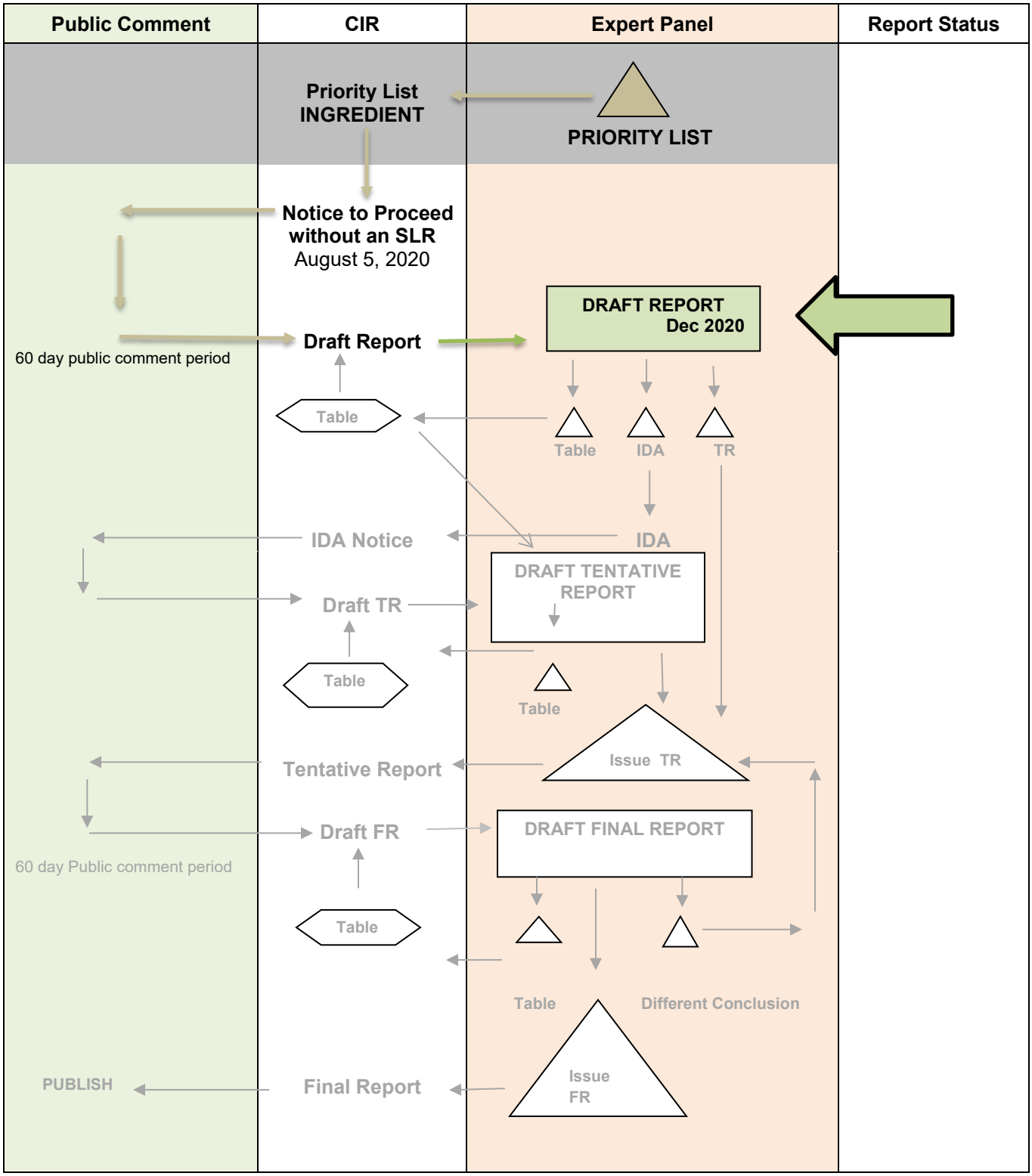
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Barley-derived Ingredients

MEETING December 2020



Barley-Derived Ingredients History

August 5, 2020 – Notice to Proceed issued.

August – October 2020 – Unpublished data received.

Barley-Derived Ingredients Data Profile* – December 2020 – Christina Burnett

					Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irritation			Dermal Sensitization				Ocular Irritation		Clinical Studies		
	Reported Use	GRAS	Method of Mfg	Constituents/ Impurities	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal/Human	Retrospective/ Multicenter	Case Reports	In-Use
Hordeum Distichon (Barley) Extract	X		X	X																										
Hordeum Distichon (Barley) Seed Flour			X	X																										
Hordeum Vulgare Extract	X																				X			X						X
Hordeum Vulgare Flower/Leaf/Stem Juice																														
Hordeum Vulgare Juice				X																										
Hordeum Vulgare Leaf Extract	X																													
Hordeum Vulgare Leaf Juice																														
Hordeum Vulgare Leaf Powder																														
Hordeum Vulgare Leaf/Stem Powder																														
Hordeum Vulgare Powder																														
Hordeum Vulgare Root Extract																														
Hordeum Vulgare Seed Extract	X		X	X																				X						
Hordeum Vulgare Seed Flour			X	X																										
Hordeum Vulgare Seed Water			X																											
Hordeum Vulgare Sprout Extract				X																										
Hordeum Vulgare Stem Water																														
Barley flour - generic	X																													
Barley - generic		X		X																									X	

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

Barley-Derived Ingredients

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

Botanical and/or Fragrance Websites (if applicable)

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

Search Strategy

PubMed

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

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

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

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

LINKS

Search Engines

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

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

Pertinent Websites

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

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

Botanical Websites, if applicable

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

Fragrance Websites, if applicable

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

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INTRODUCTION

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

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

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

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

Botanicals, such as barley-derived ingredients, may contain many constituents. However, in this assessment, the Panel will assess the safety of each of the botanical ingredients as a whole, complex mixture.

Most of the ingredients reviewed in this safety assessment may be consumed as food, and daily exposure as such would result in much larger systemic exposures than possible from use of these ingredients in cosmetic products. Therefore, the primary focus of this safety assessment is on the potential for local effects from topical exposure to these ingredients as used in cosmetics. Proteins from barley in the diet, specifically gluten, are associated with adverse health conditions (such as celiac disease) in a small portion of the general population.[5] Since the concentration of gluten in cosmetics is low, it is unlikely that enough gluten could be absorbed by the percutaneous route or by inadvertent ingestion from cosmetic products to precipitate a flare-up of either gastrointestinal or cutaneous symptoms.[6]

This safety assessment includes relevant published and unpublished data that are available for each endpoint that is evaluated. Published data are identified by conducting an exhaustive search of the world's literature. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that Panel typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

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

CHEMISTRY

Definition and Plant Identification

The definitions of the ingredients included in this review are provided in Table 1.[3] The generic CAS number for the barley ingredients in this report is 85251-64-5. Barley is the 4th most widely produced cereal grain in the world after wheat, rice, and corn.[7,8] Barley is one of the most ancient and most cultivated grains, and is more productive and stable against seasonal variations and poor soil conditions than other grains.[1,8] The origin of *Hordeum vulgare* is uncertain, but it is believed to have been domesticated in the Fertile Crescent or in east Asia nearly 10,000 - 13,000 years ago.[1,9,10] In present day, it is cultivated on all continents, except Antarctica, in temperate and tropical areas.[11]

Table 2 lists the generic definitions of the parts of plants that are most pertinent to the ingredients in this report.[3] The barley plant is an annual grass that may be either planted in the fall (winter annual variety) or in the spring (spring annual variety).[1,12] Barley sprouts are the young leaves of barley harvested approximately 10 d after sowing seeds.[10] Stems may vary in length from 1 to 4 ft, depending on variety and growing conditions. Stem are round, hollow between nodes, and

develop 5 to 7 nodes below the head. At each node, a clasping leaf develops. The spike, which contains the flowers and later the mature seeds, consists of spikelets attached to the central stem or rachis. Three spikelets develop at each node on the rachis. The barley kernel consists of the caryopsis (internal seed), the lemma (the lower bract of the floret), and palea (the upper bract of the floret). The barley kernel is generally spindle-shaped.

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

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

Chemical Properties

Horduem Vulgare Seed Extract

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

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

Method of Manufacture

Hordeum Distichon (Barley) Extract

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

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

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

Hordeum Vulgare Seed Extract

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

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

Hordeum Vulgare Seed Water

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

Composition/Impurities

Yields of constituents in barley have been found to be dependent on extraction methods and growing conditions, such as soil composition, climate, duration of growth period, and cultivar (i.e. specific genotypes, including those of different grain colors).[21-23] Additionally, different plant parts have different constituent compositions. For example, the composition of the water-soluble flavonoid, anthocyanin, varies depending on the grain color of barley (purple, black, or yellow) and on the location of the barley grain; e.g., the anthocyanin content in the outer 10% of the bran-rich kernel layers can be as much as 6 times greater than that found in the whole kernel flour.[24] Table 3 describes the phenolic composition of three different parts of two different barley cultivars.[25]

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

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

Hordeum Distichon (Barley) Extract

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

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

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

Hordeum Distichon (Barley) Seed Flour

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

Hordeum Vulgare Juice

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

Hordeum Vulgare Seed Extract

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

In another constituent analysis of a methanol extract of *Hordeum vulgare* seeds (referred to synonymously as *Hordeum sativum*), total polyphenol content was 3.67 mg/g dry weight and total flavonoid content was 2.56 mg/g dry weight.[33] In a study of extract yields in three varieties of *Hordeum vulgare*, the total phenolic content of 100% methanol extract ranged from 88.1 to 118.5 mg/100 g extract.[34] Extracts with 80% methanol had total phenolic content ranging from 980 to 145.7 mg/100 g extract.

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

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

Hordeum Vulgare Seed Flour

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

Hordeum Vulgare Sprout Extract

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

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

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

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

USE

Cosmetic

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

According to 2020 VCRP survey data, Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 383 formulations; the majority of the uses are in leave-on skin care products (Table 4).[42] Hordeum Distichon (Barley) Extract has the second greatest reported number of uses in this safety assessment with 91 formulations; the majority of the uses are also in leave-on skin care products. The remaining 2 in-use ingredients are reported to be used in much smaller numbers. The results of the concentration of use survey conducted by the Council in 2018 indicate that the highest concentration of use for Hordeum Vulgare Extract is 1.5% in leave-on body and hand skin care products.[43] According to a Council survey conducted in 2020, Hordeum Distichon (Barley) Extract is reported to be used at up to 1.8% in leave-on moisturizing products.[44] No concentrations of use were reported for any of the other barley-derived ingredients in this report. The 12 ingredients not in use, according to the VCRP and industry survey, are listed in Table 5.[42-44]

Barley-derived ingredients may be used in products that can be incidentally ingested, come in contact with mucous membranes, or be used near the eye; for example, Hordeum Vulgare Extract is reported to be used in lipsticks at 0.15% and eye makeup preparations at up to 0.075% and Hordeum Distichon (Barley) Extract is used at up to 0.3% in eye makeup preparations.[43,44] Additionally, some of the ingredients are used in cosmetic sprays and powders and could possibly be inhaled; for example, Hordeum Vulgare Extract is reported to be used at up to 0.03% in body and hand spray preparations, and at concentrations up to 0.015% in face powders.[43] In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[45,46] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[47,48] Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.[49-51]

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

Non-Cosmetic

According to the US FDA, under 21 CFR 582.20, malt extract from *Hordeum vulgare* L. (or other grains) is a substance generally recognized as safe (GRAS) in animal drugs, feeds, and related products. Roughly half of the barley grown in the US is used for livestock feed, and another quarter to a third is used for malting.[1,12] Barley for human consumption is made into pearl barley by using abrasive disks to grind the hulls and bran off the kernels.

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

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

TOXICOKINETIC STUDIES

No relevant toxicokinetics studies on barley-derived ingredients were found in the public literature, and unpublished data were not submitted. In general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

TOXICOLOGICAL STUDIES

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

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

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

GENOTOXICITY STUDIES

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

CARCINOGENICITY STUDIES

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

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Human

Hordeum Vulgare Extract

In a 48-h patch test, 20 subjects received a product containing 0.005% Hordeum Vulgare Extract (undiluted) via occlusive patches on the back.[63] The test sites were examined at 15 min and 24 h after patch removal. Two subjects had a erythema score of 1 at 15 min, with one of the subjects continuing to have the same score at 24 h. The average irritation index was determined to be 0.1 at 15 min and 0.05 at 24 h. It was concluded that the test material was not irritating.

Sensitization

Human

Hordeum Vulgare Extract

The dermal sensitization potential of a face mask formulation containing 0.005% Hordeum Vulgare Extract was evaluated in a human repeated insult patch test (HRIPT) in 110 subjects.[64] The subjects received approximately 0.2 g of the test material on the upper back via a 1 in^2 absorbent pad with clear adhesive dressing as a semi-occlusive patch. The patches were applied 3 times/wk for a total of 9 applications during the induction phase. After a 2-wk rest period, the subjects received a challenge patch on a virgin test site adjacent to the induction sites. Test sites were scored on day 1 and day 3 post-application. No signs of irritation or sensitization to the test material were observed. It was concluded that the test material was not a dermal irritant or sensitizer.

In another HRIPT following a similar protocol, the dermal sensitization potential of a pressed powder containing 0.005% Hordeum Vulgare Extract was assess in 107 subjects.[65] Test patches were moistened with several drops of water to

ensure adherence of the test material. No signs of irritation or sensitization to the test material were observed. It was concluded that the test material was not a dermal irritant or sensitizer.

Hordeum Vulgare Seed Extract

In a HRIPT that assessed contact irritation and/or sensitization of a skin serum formulation containing 0.1% Hordeum Vulgare Seed Extract, 50 subjects received the test material under occlusive patches.[66] The test was performed in the manner previously described. No adverse reactions were induced during the course of the study. The skin serum containing 0.1% Hordeum Vulgare Seed Extract was considered to be non-irritating and non-sensitizing.

OCULAR IRRITATION STUDIES

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

CLINICAL STUDIES

Ocular In-Use Studies

Hordeum 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.[67] 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 both contact and 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.[68] 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-year-old malt worker at a silo presented with eczema on the fingers of both hands.[69] 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.[70] 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.[71-74] 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.[71,73,74] 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.[71,73,74] 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.[72] 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.[75-77] Food allergy to barley has been reported; in Korean children, evidence of cross-reactivity or co-sensitization with wheat has been found.[78,79]

SUMMARY

Hordeum distichon and *Hordeum vulgare* are two species of barley, an annual grass, that is cultivated as a cereal grain. Most of the 16 barley-derived ingredients detailed in this safety assessment are reported to function in cosmetics as skin conditioning agents, while some are reported to have other functions, such as abrasives, antioxidants, and bulking agents. The Panel has reviewed the safety of Hydrolyzed Barley Protein, and concluded that this ingredient is safe in cosmetics in the present practices of use and concentration.

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

According to 2020 VCRP survey data, Hordeum Vulgare Extract has the most reported uses in cosmetic products, with a total of 383 formulations; the majority of the uses are in leave-on skin care products. Hordeum Distichon (Barley) Extract has the second greatest reported number of uses in this safety assessment with 91 formulations; the majority of the uses are also in leave-on skin care products. The remaining 2 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 12 barley-derived ingredients in this report.

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

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

Hordeum Vulgare Extract (0.005%) in an undiluted product was not irritating in a 48-h patch test in 20 subjects. No irritation or sensitization was observed in HRIPTs of a face mask product or in a pressed powder product, each containing 0.005% Hordeum Vulgare Extract. Hordeum Vulgare Seed Extract (0.1% in a skin serum formulation) was not a dermal irritant or dermal sensitizer in an HRIPT. An eye cream containing 0.005% Hordeum Vulgare Extract was determined not to be an ocular irritant in an in-use study.

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

DISCUSSION

To be determined…

CONCLUSION

To be determined…

TABLES

Table 1. Definitions and functions of the ingredients in this safety assessment.[3]

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

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

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

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

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

Table 4. Frequency (2020)[42] and concentration (2018;[43] 2020[44]) of use according to duration and type of exposure for barley-derived ingredients[42-44]

	# of Uses[42]	*Max Conc of Use (%)*[44]	*# of Uses*[42]	*Max Conc of Use (%)*[43]	*# of Uses*[42]	*Max Conc of Use (%)*[43]	*# of Uses*[42]	*Max Conc of Use (%)*[43]
	Hordeum Distichon (Barley) Extract		**Hordeum Vulgare Extract**		**Hordeum Vulgare Leaf Extract**		**Hordeum Vulgare Seed Extract**	
Totals†	**91**	**0.005-1.8**	**383**	**0.000015-1.5**	**2**	**NR**	**34**	**NR**
Duration of Use								
Leave-On	73	0.005-1.8	328	0.000015-1.5	2	NR	31	NR
Rinse Off	18	0.1	54	0.0015-0.15	NR	NR	3	NR
Diluted for (Bath) Use	NR	NR	1	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	6	0.005-0.3	40	0.005-0.075	1	NR	1	NR
Incidental Ingestion	2	NR	20	0.15	NR	NR	NR	NR
Incidental Inhalation-Spray	26[a,b]	NR	7; 179[a]; 39[b]	0.03; 0.03-0.038[a]; 0.03[b]	1[b]	NR	11; 4[a]; 15[b]	NR
Incidental Inhalation-Powder	2; 26[b]	0.005[c]	7; 39[b]; 2[c]	0.15; 0.03[b]; 0.001-1.5[c]	1[b]	NR	15[b]	NR
Dermal Contact	74	0.005-1.8	352	0.000015-1.5	2	NR	34	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	14	NR	11	0.0015-0.038	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	1	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	5	NR	41	0.15	NR	NR	NR	NR
Baby Products	NR	NR	2	NR	NR	NR	NR	NR

	Barley Flour* [42]	
Totals†	**1**	**
Duration of Use		
Leave-On	NR	**
Rinse Off	1	**
Diluted for (Bath) Use	NR	**
Exposure Type		
Eye Area	NR	**
Incidental Ingestion	NR	**
Incidental Inhalation-Spray	NR	**
Incidental Inhalation-Powder	NR	**
Dermal Contact	1	**
Deodorant (underarm)	NR	**
Hair - Non-Coloring	NR	**
Hair-Coloring	NR	**
Nail	NR	**
Mucous Membrane	1	**
Baby Products	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.

* VCRP data was listed generically as barley flour and did not distinguish species.

** Not an INCI ingredient: concentration of use survey under this name was not conducted.

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 5. Ingredients not reported in use.[42-44]

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

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2020 FDA VCRP Raw Data

HORDEUM DISTICHON (BARLEY) EXTRACT	03D	Eye Lotion	6
HORDEUM DISTICHON (BARLEY) EXTRACT	05A	Hair Conditioner	8
HORDEUM DISTICHON (BARLEY) EXTRACT	05F	Shampoos (non-coloring)	3
HORDEUM DISTICHON (BARLEY) EXTRACT	05G	Tonics, Dressings, and Other Hair Grooming Aids	3
HORDEUM DISTICHON (BARLEY) EXTRACT	07B	Face Powders	2
HORDEUM DISTICHON (BARLEY) EXTRACT	07C	Foundations	2
HORDEUM DISTICHON (BARLEY) EXTRACT	07E	Lipstick	2
HORDEUM DISTICHON (BARLEY) EXTRACT	07H	Makeup Fixatives	1
HORDEUM DISTICHON (BARLEY) EXTRACT	07I	Other Makeup Preparations	3
HORDEUM DISTICHON (BARLEY) EXTRACT	08C	Nail Creams and Lotions	1
HORDEUM DISTICHON (BARLEY) EXTRACT	10A	Bath Soaps and Detergents	2
HORDEUM DISTICHON (BARLEY) EXTRACT	10E	Other Personal Cleanliness Products	1
HORDEUM DISTICHON (BARLEY) EXTRACT	11A	Aftershave Lotion	1
HORDEUM DISTICHON (BARLEY) EXTRACT	11E	Shaving Cream	1
HORDEUM DISTICHON (BARLEY) EXTRACT	12A	Cleansing	2
HORDEUM DISTICHON (BARLEY) EXTRACT	12C	Face and Neck (exc shave)	18
HORDEUM DISTICHON (BARLEY) EXTRACT	12D	Body and Hand (exc shave)	8
HORDEUM DISTICHON (BARLEY) EXTRACT	12F	Moisturizing	18
HORDEUM DISTICHON (BARLEY) EXTRACT	12G	Night	2
HORDEUM DISTICHON (BARLEY) EXTRACT	12H	Paste Masks (mud packs)	1
HORDEUM DISTICHON (BARLEY) EXTRACT	12J	Other Skin Care Preps	3
HORDEUM DISTICHON (BARLEY) EXTRACT	13B	Indoor Tanning Preparations	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	02D	Other Bath Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	03C	Eye Shadow	7
HORDEUM VULGARE (BARLEY) EXTRACT	03D	Eye Lotion	24
HORDEUM VULGARE (BARLEY) EXTRACT	03E	Eye Makeup Remover	1
HORDEUM VULGARE (BARLEY) EXTRACT	03G	Other Eye Makeup Preparations	8
HORDEUM VULGARE (BARLEY) EXTRACT	04E	Other Fragrance Preparation	7
HORDEUM VULGARE (BARLEY) EXTRACT	05A	Hair Conditioner	3
HORDEUM VULGARE (BARLEY) EXTRACT	05F	Shampoos (non-coloring)	4
HORDEUM VULGARE (BARLEY) EXTRACT	05G	Tonics, Dressings, and Other Hair Grooming Aids	3
HORDEUM VULGARE (BARLEY) EXTRACT	05I	Other Hair Preparations	1
HORDEUM VULGARE (BARLEY) EXTRACT	07A	Blushers (all types)	5
HORDEUM VULGARE (BARLEY) EXTRACT	07B	Face Powders	7
HORDEUM VULGARE (BARLEY) EXTRACT	07C	Foundations	6
HORDEUM VULGARE (BARLEY) EXTRACT	07E	Lipstick	20
HORDEUM VULGARE (BARLEY) EXTRACT	07I	Other Makeup Preparations	4

HORDEUM VULGARE (BARLEY) EXTRACT	10A	Bath Soaps and Detergents	20
HORDEUM VULGARE (BARLEY) EXTRACT	12A	Cleansing	26
HORDEUM VULGARE (BARLEY) EXTRACT	12C	Face and Neck (exc shave)	18
HORDEUM VULGARE (BARLEY) EXTRACT	12D	Body and Hand (exc shave)	21
HORDEUM VULGARE (BARLEY) EXTRACT	12F	Moisturizing	148
HORDEUM VULGARE (BARLEY) EXTRACT	12G	Night	17
HORDEUM VULGARE (BARLEY) EXTRACT	12H	Paste Masks (mud packs)	5
HORDEUM VULGARE (BARLEY) EXTRACT	12J	Other Skin Care Preps	19
HORDEUM VULGARE (BARLEY) EXTRACT	13B	Indoor Tanning Preparations	5
HORDEUM VULGARE (BARLEY) EXTRACT	13C	Other Suntan Preparations	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	03D	Eye Lotion	1
HORDEUM VULGARE (BARLEY) LEAF EXTRACT	12C	Face and Neck (exc shave)	1
HORDEUM VULGARE (BARLEY) SEED EXTRACT	03D	Eye Lotion	1
HORDEUM VULGARE (BARLEY) SEED EXTRACT	04E	Other Fragrance Preparation	11
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12A	Cleansing	3
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12C	Face and Neck (exc shave)	15
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12F	Moisturizing	3
HORDEUM VULGARE (BARLEY) SEED EXTRACT	12I	Skin Fresheners	1
BARLEY FLOUR	10A	Bath Soaps and Detergents	1

Concentration of Use by FDA Product Category – Barley-Derived Ingredients*

Hordeum Vulgare Extract
Hordeum Vulgare Flower/Leaf/Stem Juice
Hordeum Vulgare Juice
Hordeum Vulgare Leaf Extract
Hordeum Vulgare Leaf Juice
Hordeum Vulgare Leaf Powder
Hordeum Vulgare Leaf/Stem Powder
Hordeum Vulgare Powder
Hordeum Vulgare Root Extract
Hordeum Vulgare Seed Extract
Hordeum Vulgare Seed Flour
Hordeum Vulgare Seed Water
Hordeum Vulgare Sprout Extract
Hordeum Vulgare Stem Water

Ingredient	Product Category	Maximum Concentration of Use
Hordeum Vulgare Extract	Eye shadows	0.015%
Hordeum Vulgare Extract	Eye lotions	0.005-0.075%
Hordeum Vulgare Extract	Hair conditioners	0.006%
Hordeum Vulgare Extract	Shampoos (noncoloring)	0.0015%
Hordeum Vulgare Extract	Tonics, dressings and other hair grooming aids	0.038%
Hordeum Vulgare Extract	Blushers	0.000015-0.001%
Hordeum Vulgare Extract	Face powders	0.015%
Hordeum Vulgare Extract	Foundations	0.005-0.12%
Hordeum Vulgare Extract	Lipstick	0.15%
Hordeum Vulgare Extract	Other makeup preparations	0.005%
Hordeum Vulgare Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.075%
Hordeum Vulgare Extract	Face and neck products Not spray	 0.001-0.075%
Hordeum Vulgare Extract	Body and hand products Not spray Spray	 0.03-1.5% 0.03%
Hordeum Vulgare Extract	Foot powders and spray	0.03%
Hordeum Vulgare Extract	Moisturizing products Not spray	 0.03%
Hordeum Vulgare Extract	Night products Not spray	 0.005%
Hordeum Vulgare Extract	Paste masks and mud packs	0.005-0.15%
Hordeum Vulgare Extract	Other skin care preparations	0.03%
Hordeum Vulgare Extract	Suntan products Not spray	 0.075%
Hordeum Vulgare Extract	Other suntan preparations	0.03%

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

Information collected in 2018
Table prepared May 31, 2018

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: August 12, 2020

SUBJECT: Hordeum Vulgare Seed Extract

CEP - Solabia Group. 2010. Ingredient breakdown Barley Milk 1.5PS.

CEP - Solabia Group. 2010. Manufacturing process Barley Milk 1.5PS.

CEP - Solabia Group. 2016. Specifications data sheet Barley Milk 1.5PS.

CEP - Solabia Group. 2010. Ingredient breakdown Three Cereals Milk 1.5PS.

CEP - Solabia Group. 2010. Manufacturing process Three Cereals Milk 1.5PS.

CEP - Solabia Group. 2015. Specifications data sheet Three Cereals Milk 1.5PS.

INGREDIENT BREAKDOWN
COMPOSITION CENTESIMALE

Barley Milk 1.5PS
Lait d'Orge 1,5PS

Ref. FL530

Water	**94.90 %**
Hordeum vulgare seed extract *3g under halogen, 1 hour at 110°C.*	**3.00 %**
Phenoxyethanol	**1.50 %**
Xanthan gum	**0.30 %**
Potassium sorbate	**0.30 %**

Notes - *Remarques :*

- Because of the natural origin of the raw material, the centesimal composition is susceptible to slight variations.

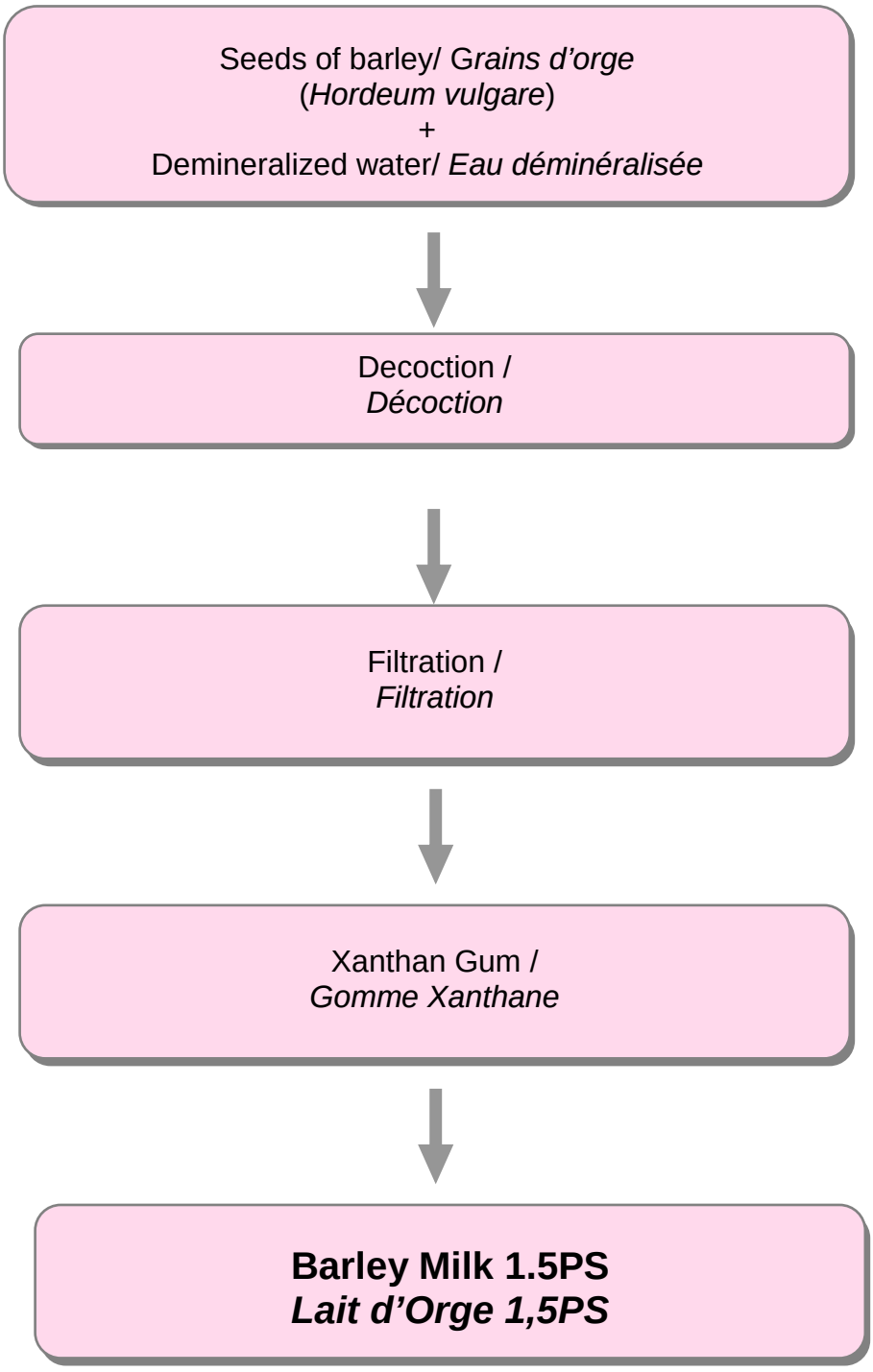
  En raison de l'origine naturelle des matières premières, la composition centésimale est susceptible de subir une légère variation.

Produced & Commercialized by CEP - SOLABIA Group
29 Rue Delizy – 93698 Pantin Cedex France
Tel 33 (0)1 48 10 19 40 – Fax 33 (0)1 48 91 18 77 - www.solabia.com

MANUFACTURING PROCESS
PROCEDE DE FABRICATION

Barley Milk 1.5PS
Lait d'Orge 1,5PS

Ref. FL530



Produced & Commercialized by CEP - SOLABIA Group
29 Rue Delizy – 93698 Pantin Cedex France
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SPECIFICATIONS DATA SHEET

Barley Milk 1.5PS

Ref. FL530

DEFINITION

Barley Milk 1.5PS is a milky preparation, combining liposoluble fraction and the water-soluble fraction of the seeds of barley (*Hordeum vulgare).*

PRESENTATION

• **Sample**	plastic flask - 125 mL
• **Code / Packaging** *to be mentioned with your order*	FL530KC - can 5 kg FL530KE - can 20 kg

ORGANOLEPTIC CHARACTERISTICS

• **Appearance**	opaque solution
• **Color**	ivory
• **Odor**	characteristic

ANALYTICAL CHARACTERISTICS

• **pH**	3.5 – 4.7
• **Refractive index at 20°C**	1.335 - 1.342
• **Dry extract** *3g under halogen, 1 hour at 110°C*	2.7 - 3.7%

MICROBIOLOGICAL CHARACTERISTICS

• **Total aerobic microbial count** *Eur. Ph. 8th ed. § 2.6.12 – 2.6.13*	≤ 100 C.F.U/g

Barley Milk 1.5PS

Additional Analysis

- **Content of sugars** 38.8 g/L
- **Total nitrogen** 0.42 g/L

Solubilities (10% diluted)

- **Water** miscible
- **Alcohol 50% v/v** miscible
- **Mineral oils** non miscible
- **Vegetal oils** non miscible

Storage and use

- **Shelf life** 3 years in closed original packaging.
- **Preservative system** 1.5% of phenoxyethanol, 0.3% of potassium sorbate
- **Storage conditions** store at room temperature
  There may be a slight phase separation after several months of storage.
- **Use conditions** mix before use if necessary

Legislative Information

- **INCI** Aqua / Hordeum vulgare extract/ Xanthan Gum
- **CTFA** Water (and) Hordeum vulgare seed extract (and) Xanthan gum
- **CAS**

Aqua	7732-18-5
Hordeum vulgare extract	85251-64-5
Xanthan gum	11138-66-2

- **EINECS**

Aqua	231-791-2
Hordeum vulgare extract	286-476-2
Xanthan gum	234-394-2

Produced & Commercialized by CEP - SOLABIA Group
29 Rue Delizy – 93698 Pantin Cedex France
Tel 33 (0)1 48 10 19 40 – Fax 33 (0)1 48 91 18 77 - www.solabia.com

INGREDIENT BREAKDOWN
COMPOSITION CENTESIMALE

Three Cereals Milk 1.5PS
Lait aux Trois Céréales 1,5PS

Ref. FL544

Water ..... **94.90 %**

Avena sativa (oat) kernel extract (and)
Triticum vulgare (wheat) seed extract (and)
Hordeum vulgare seed extract ..... **3.00 %**
3g under halogen, 1 hour at 110°C.

Phenoxyethanol ..... **1.50 %**

Xanthan gum..... **0.30 %**

Potassium sorbate ..... **0.30 %**

Notes - *Remarques:*

- Because of the natural origin of the raw material, the centesimal composition is susceptible to slight variations.

  En raison de l'origine naturelle des matières premières, la composition centésimale est susceptible de subir une légère variation.

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MANUFACTURING PROCESS
PROCEDE DE FABRICATION

Three Cereals Milk 1.5PS
Lait aux Trois Céréales 1,5PS

Ref. FL544

Crushed seeds of oat / *Graines broyées d'avoine* (*Avena sativa*)
Crushed seeds of wheat / *Graines broyées de blé* (*Triticum vulgare*)
Crushed seeds of barley / *Graines broyées d'orge* (*Hordeum vulgare*)

↓

Warm aqueous co-extraction /
Co-extraction aqueuse à chaud

↓

Xanthan gum /
Gomme xanthane

↓

Three Cereals Milk 1.5PS
Lait aux Trois Céréales 1,5PS

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SPECIFICATIONS DATA SHEET

Three Cereals Milk 1.5PS

Ref. FL544

DEFINITION

Three Cereals Milk 1.5PS is a milky preparation, combining liposoluble and water-soluble fractions of the crushed seeds of:

- Oat (*Avena sativa*)
- Wheat (*Triticum vulgare*)
- Barley (*Hordeum vulgare*)

PRESENTATION

Sample	plastic flask - 125 mL
Code / Packaging *to be mentioned with your order*	FL544KC - can 5 kg FL544KE - can 20 kg

ORGANOLEPTIC CHARACTERISTICS

Appearance	opaque solution
Color	grey yellow
Odor	characteristic

ANALYTICAL CHARACTERISTICS

pH MODIFICATION	3.0 - 5.0
Refractive index at 20°C MODIFICATION	1.330 - 1.350
Dry Extract MODIFICATION *3g under halogen, 1 hour at 110°C*	2.5% - 4.0%

MICROBIOLOGICAL CHARACTERISTICS

Total aerobic microbial count *Eur. Ph. 8th ed. § 2.6.12 – 2.6.13*	≤ 100 C.F.U/g

Three Cereals Milk 1.5PS

SOLUBILITIES

• **Water**	miscible	• **Mineral oils**	non miscible
• **Alcohol 50% v/v**	miscible	• **Vegetal oils**	non miscible

STORAGE AND USE

- **Shelf life**: 3 years in closed original packaging
- **Preservative system**: 1.5% of phenoxyethanol, 0.3% of potassium sorbate
- **Storage conditions**: store at room temperature,
  There may be a slight separation after several months of storage
- **Use conditions**: mix before use if necessary
  .

LEGISLATIVE INFORMATION

- **INCI**: Aqua / Avena sativa kernel extract / Triticum vulgare extract / Hordeum vulgare extract / Xanthan gum
- **CTFA**: Water (and) Avena sativa (oat) kernel extract (and) Triticum vulgare (wheat) seed extract (and) Hordeum vulgare seed extract (and) Xanthan gum
- **CAS**:

Water	7732-18-5
Avena sativa kernel extract	84012-26-0
Triticum vulgare extract	84012-44-2
Hordeum vulgare extract	85251-64-5
Xanthan gum	11138-66-2

- **EINECS**:

Water	231-791-2
Avena sativa kernel extract	281-672-4
Triticum vulgare extract	281-689-7
Hordeum vulgare extract	286-476-2
Xanthan gum	234-394-4

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Tel 33 (0)1 48 10 19 40 – Fax 33 (0)1 48 91 18 77 - www.solabia.com

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: August 14, 2020

SUBJECT: Hordeum Distichon (Barley) Extract

Anonymous. 2020. Hordeum Distichon (Barley) Extract: Method of manufacture and impurities.

- **Hordeum Distichon (Barley) Extract**

Manufacturing Process:

The barley is extracted with specified **eluent(s) under appropriate temperature conditions,** to yield a **concentrate**. The concentrate containing the phytochemical constituents is then blended with the desired diluent(s) and preservation system to produce the final ingredient. The ingredient is evaluated for physiochemical properties according to the specification requirements for the batch to be released. In addition, the concentrate is also evaluated for contaminants and physiochemical properties as needed.

Typical eluents include Water, Butylene Glycol, Carthamus Tinctorius (Safflower) Seed Oil, Glycerin, and Propylene Glycol.

Heavy Metal & Pesticides/ Allergens/ Impurities:

The following heavy metal testing was conducted on the concentrate in an alcohol base:

Heavy metals:	**Heavy Metal**	**Detection**	**Reporting Limit**	**Heavy Metal**	**Detection**	**Reporting Limit**
	Antimony	Not Detected	0.01 mg/l	Iron	Not Detected	0.1 mg/l
	Arsenic	Not Detected	0.01 mg/l	Lead	Not Detected	0.0025 mg/l
	Cadmium	Not Detected	0.001 mg/l	Mercury	Not Detected	0.0002 mg/l
	Chromium	Not Detected	0.002 mg/l	Nickel	Not Detected	0.002 mg/l

There were no residual pesticides detected. (Parameters: 8081 GCS Pesticides and 8141 GCS, O/P Pesticides)

The following Allergen testing was conducted on the concentrate in an alcohol base:

Presence of the 26 allergens defined by the 7th amendment to the EU Cosmetic Directive:	**Fragrance Ingredient**	**Threshold**	**Fragrance Ingredient**	**Threshold**
	Amyl Cinnamal	<10ppm-0.001%	Anise Alcohol	<10ppm-0.001%
	Benzyl Alcohol	<10ppm-0.001%	Benzyl Cinnamate	<10ppm-0.001%
	Cinnamyl Alcohol	<10ppm-0.001%	Farnesol	<10ppm-0.001%
	Citral	<10ppm-0.001%	Butylphenyl Methylpropional	<10ppm-0.001%
	Eugenol	<10ppm-0.001%	Linalool	<10ppm-0.001%
	Hydroxycitronellal	<10ppm-0.001%	Benzyl Benzoate	<10ppm-0.001%
	Isoeugenol	<10ppm-0.001%	Citronellol	<10ppm-0.001%
	Amylcinnamyl Alcohol	<10ppm-0.001%	Hexyl Cinnamal	<10ppm-0.001%
	Benzyl Salicylate	<10ppm-0.001%	Limonene	<10ppm-0.001%
	Cinnamal	<10ppm-0.001%	Methyl l2-octynoate	<10ppm-0.001%
	Hydroxyisohexyl 3-Cyclohexene Carboxaldehyde	<10ppm-0.001%	Alpha-Isomethyl Inone (Other Name: Methyl Lonone Gamma)	<10ppm-0.001%
	Coumarin	<10ppm-0.001%	Evernia Prunastri (Oak Moss) Extract	Not Tested
	Geraniol	<10ppm-0.001%	Evernia Furfuracea (Tree Moss) Extract	Not Tested

*The given values correspond to the limit of determination OR *Results have been calculated form highest reported values published.

Personal Care Products Council
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Memorandum

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

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

DATE: August 25, 2020

SUBJECT: Hordeum Vulgare Seed Water

Anonymous. 2020. Method of manufacture Hordeum Vulgare Seed Water.

August 2020

Method of Manufacture Hordeum Vulgare Seed Water

Hordeum Vulgare seed water is obtained from the seed of barley by steam distillate.

Starting material: Dry seed and steam (water vapor).

Steam distillation is carried out up to a ratio dry seed/distillate of 40%.

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: October 5, 2020

SUBJECT: Hordeum Vulgare Seed Extract

ORF Genetics. 2020. Product information sheet - Barley Seed Extract (INCI: Hordeum Vulgare Seed Extract).

ORF Genetics. 2020. Material safety data sheet - Barley Seed Extract (INCI: Hordeum Vulgare Seed Extract).

ORF Genetics. 2020. Pesticide analyzes results- Pesticide analysis on barley seed extract freeze-dried powder.

Bioeffect EHF. 2019. Certificate of manufacturing - Bioeffect EGF serum (contains 0.1% Hordeum Vulgare Seed Extract).

Bioeffect EHF. 2020. QA report Oct2020; No undesirable effects reported on BIOEFFECT products.

ORF Genetics
Vikurhvarf 7
Kopavogur, Iceland
Tel: + 354 531 1000
Fax: + 354 531 1001

PRODUCT INFORMATION SHEET

02.10.2020

Product

Barley Seed Extract

INCI; *Hordeum Vulgare Seed Extract*

Content

- Product and Manufacturer information
- Definition of Ingredients Source
- Manufacturing flow chart, including method description of extract purification and sterilization.

Additional Product Information Documents - available upon request

- MSDS (Material Safety Data Sheet) for the Barley Seed Extract
- Certificate of Manufacturing for the product BIOEFFECT EGF SERUM
- Pesticide Analysing Results (Report on Pesticides Measurements)
- Report from hRIPT study conducted by AMA Laboratories (MS11.RIPT.L99110.50.CJHI)
- QA report Oct 2020: No serious undesirable effects reported on BIOEFFECT products.

Prepared by:

2/10/20 Hilmar Vidarsson

Hilmar Vidarsson
Regulatory Compliance Officer
ORF Genetics and BIOEFFECT

Product and Manufacturer Information

Product: Barley Seed Extract, *freeze dried powder*

INCI Name: *Hordeum Vulgare Seed Extract*

Description of INCI *(from CosIng; the European Commission database for information on cosmetic substances and ingredients contained in Cosmetics Regulation (EC) No 1223/2009 of the European Parliament)*

Total: 1

#	INCI Name/Substance Name	CAS No.	EC No.	Restriction/ Annex/Ref #
1.	HORDEUM VULGARE SEED EXTRACT	85251-64-5	286-476-2	

Total: 1

Description: *As described in CosIng; the European Commission database for information on cosmetic substances and ingredients contained in Cosmetics Regulation (EC) No 1223/2009 of the European Parliament*

INCI Name	HORDEUM VULGARE SEED EXTRACT
Description	Hordeum Vulgare Seed Extract is an extract of the seeds of the Barley, Hordeum vulgare L., Graminae
CAS #	85251-64-5
EC #	286-476-2
Cosmetics Regulation provisions	
Functions	• SKIN CONDITIONING
SCCS opinions	
Identified INGREDIENTS or substances e.g.	

MANUFACTURER

Manufacturer: ORF Genetics ehf.,

Phone: +354 531 1000
info@orfgenetics.com

Manufacturing location: Vikurhvarf 7
Kopavogur, Iceland

Facility size: 1500 m^2
Operations: Manufacturing, packaging, warehousing, distribution

Definition of Ingredients Sources

Definition of the Plant Derived Ingredients: *Hordeum Vulgare seed extract*

Starting Material: Aqueous extract of seeds

Plant Species: *Hordeum Vulgare* (barley).

Part of plant used: Seed

Country of Origin: Iceland

Characterization of the Barley seed extract *(Horderum Vulgare Seed Extract)*

The mature barley (*Hordeum Vulgare*) seed consists of the plant embryo, together with the endosperm tissue, which stores nutrition in form of carbohydrates and proteins for supporting embryo development. The storage proteins found in the seed are usually classified in four groups according to their solubility criteria (i.e. albumins, globulins, prolamins and glutelins), by which they can be specifically extracted from other seed elements. In barley the major storage proteins are the hordeins (*prolamins*) and glutelins, and together they account for up to 70% of the total protein fraction of the mature seed. Albumins and globulins each representing about 10% of the total protein content of the barley seed extract. The endosperm comprises the starchy endosperm, which is a non-living storage tissue, surrounded by a living non-starch cell layer called aleurone. The grain is protected by an outer husk.

Manufacturing process in brief *(see also Manufacturer Flow Chard on next page):*

The barley plant is cultivated in ORFs greenhouse* and after harvest the seeds go through seed processing, including drying, threshing and cleaning. Thereafter, the seeds are milled, and this serves as the starting material for the generation of the Barley seed extract that is used in skin care products.

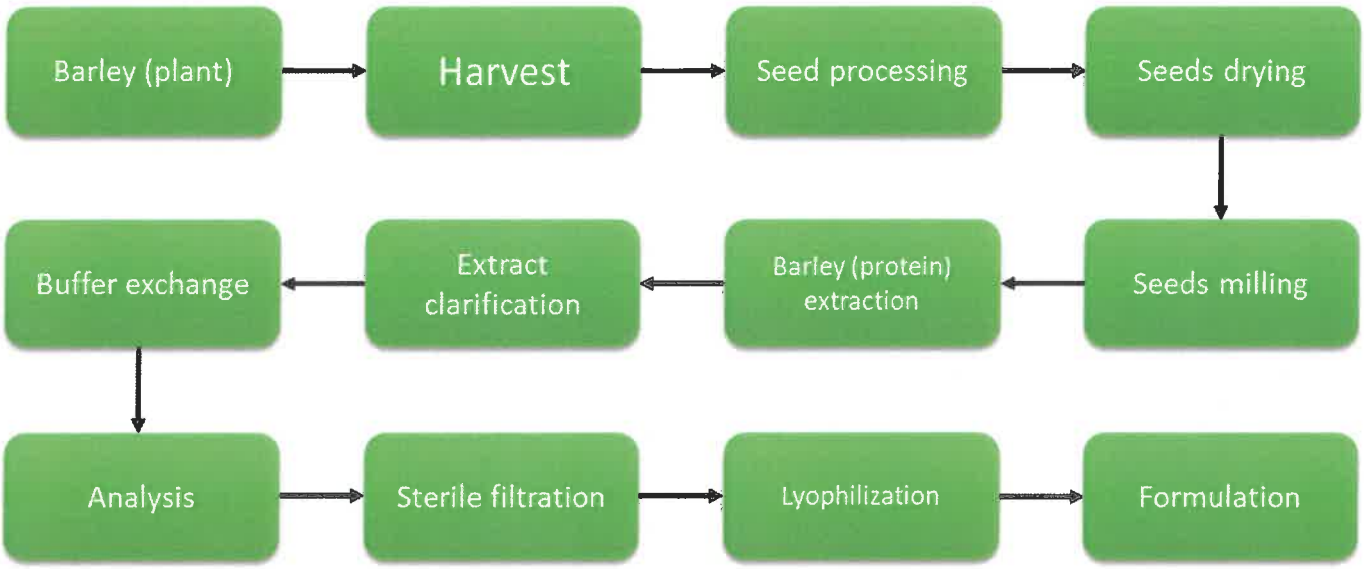
The down-stream processing starts with extraction from the milled barley seeds. The extraction is performed with standard protein extraction buffers, containing the buffering ions and sodium chloride (NaCl) at the appropriate pH for the extraction purpose. During this step the water-soluble barley proteins are pulled to the aqueous phase. Then the barley protein extract is centrifuged to separate the slurry from the aqueous phase which is collected for further clarification with the purpose of eliminating further insoluble and unwanted particles. The clarification prosses consist of different stages of filtration with Tangential Flow Filtration (TFF) technology and other filtration. After the clarification the barley extract undergoes buffer exchange required for the final formulation. Protein analysis is conducted prior to sterile filtration and lyophilization.

*** ORFs Greenhouse**

ORFs greenhouse is a 2000m2 state-of-the-art geothermally powered greenhouse where the barley plants are grown in hydroponic cultivation on conveyor belts. The nutrition, light and heat are all controlled by sensors and automated.

Manufacturing Flow Chart

Workflow:



Sterilization method prior to packaging and shipment: Sterile filtration through a 0.2 µ steritop filter from millipore (*Cat No: S2GPT05RE (500mL)*).

Hilmar Viðarsson, Regulatory Compliance

ORF Genetics
Vikurhvarf 7
Kopavogur, Iceland
Tel: + 354 531 1000
Fax: + 354 531 1001

MATERIAL SAFETY DATA SHEET

DATE: 29/9/2020

1. PRODUCT AND COMPANY IDENTIFICATION

Products Name	BARLEY SEED EXTRACT
INCI Name	Hordeum Vulgare Seed Extract
Source	*Hordeum Vulgare (Barley)*
CAS #	85251-64-5
EC #	286-476-2
Application	Chemical for various cosmetic applications

MANUFACTURER: ORF Genetics

Street address	Vikurhvarf 7
City, Postal Code	Kopavogur, 203
Country	Iceland
Telephone Number	+354 531 1000
Date:	29.9.2020
Mail:	info@orfgenetics.com

2. COMPOSITION/INFORMATION ON RESTRICTED COSMETIC INGREDIENTS

This product is a freeze-dried extract, composed of following components:

Ingredient	INCI Name	CAS	EC No.	Function
Natrium Chloride / NaCl	Sodium Chloride	7647-14-5	7647-14-5 / 231-598-3	Buffering agent
Tris / Tromethamine	Tromethamine	77-86-1	77-86-1 / 201-064-4	Buffering agent
Barley Seed Extract	Hordeum vulgare seed extract	85251-64-5	85251-64-5 / 286-476-2	Skin conditioning

Concentration of restricted ingredients in a cosmetic formulation of 1ppm Barley Seed Extract

Ingredients with restrictions	CAS No.	Conc. (%)	Function	Cosmetic regulatory summary
Tromethamine	77-86-1	0.038%	buffering agent	Maximum nitrosamine 0,5%

3. HAZARDS IDENTIFICATION

Classification of the substance or mixture: This preparation is not classified dangerous according to the criteria of European Directives 67/548/EEC or 1999/45/EC.
Not classified according to the Regulation (EC) No. 1272/2008
Label elements:

Not relevant
Not classified

Other hazards:

Lyophilized powder and thus may cause irritation to eyes and respiration tract. Use face mask and protect eyes while resuspending in liquid.

4. FIRST AID MEASURES

After contact with eyes: Rinse with water. If irritation occurs and persists, seek medical advice.
After contact with the skin: In case of allergic skin reaction or irritation, rinse with water. If irritation persists, seek medical advice.
Inhalation: Move patient to fresh air. If discomfort occurs, seek medical attention.
After swallowing: Does not induce vomiting. Rinse mouth with water. No immediate danger. Get medical advice.

5. FIRE FIGHTING MEASURES

Suitable extinguishing media: Water, CO2, Powder.
Special hazard arising from the substance or mixture: None. Non-flammable and non-explosive product.
Advice for fire-fighters: None.

6. ACCIDENTAL RELEASE MEASURES

Personal protection, protective equipment and emergency procedures: Avoid skin/eye contact. Gloves can be carried.
Environmental precautions: Collect in a suitable container.
Method and material for containment and cleaning up: Collect the product manually, wipe then rinse with water

7. HANDLING AND STORAGE

Precaution for safe handling:

Manipulation: None.
Ventilation: None

Conditions for safe storage, including any incompatibilities:

Storage conditions: Avoid humidity. Avoid excessive heat, open flames or other sources of ignition. Avoid contact with strong acids, alkalis and oxidizing agents.

Specific end use(s): Strictly respect the instructions for use.

8. EXPOSURE CONTROL / PERSONAL PROTECTION

Control parameters: None.
Exposure controls: If desired, wash hands after use.
Appropriate engineering controls: No specific measures
Environmental protection measures, such as personal protective equipment:

a) Respiratory protection: Not concerned
b) Hands protection: Gloves can be carried
c) Eyes protection: Avoid contact with eyes.

Environment exposure controls: Apply local regulations concerning the recycling and disposal of materials and packaging.

9. PHYSICAL AND CHEMICAL PROPERTIES

PARAMETERS	SPECIFICATIONS
PHYSICAL STATE	Lyophilized powder
APPEARANCE	White odourless powder
pH DETERMINATION	7.2 in solution before lyophilization
STABILITY	Stable at room temperature
MELTING POINTS	No data available
EVAPORATION RATE	No data available
BOILING POINT	No data available
VAPOUR DENSITY	No data available
SOLUBILITY	No data available
OTHER DATA	None

10. STABILITY AND REACTIVITY

Reactivity :	Product nonreactive under normal conditions of handling and storage
Chemical stability :	Product stable under normal conditions of handling and storage.
Possibility of hazardous reactions :	Under normal handling and storage, hazardous reactions will not occur .
Conditions to avoid :	Avoid long-term storage in humidity and excessive heat.
Incompatible materials :	Avoid strong acids and strong bases.
Hazardous decomposition products :	None

11. TOXICOLOGICAL INFORMATION

Toxicology data overtaken from BIOEFFECT EGF SERUM, a facial skin care product manufactured by BIOEFFECT EHF, a daughter company of ORF Genetics. The BIOEFFECT EGF SERUM is a glycerol-based serum product containing less than 1.0% (< 1.0%) Barley Seed Extract (Ref 1). Our own experience has provided no indication of any hazardous potential of this ingredient.

Oral Toxicity	Barley is considered safe as food ingredient. No own tests. Toxic reactions are not to be expected.
Eye irritation	Lyophilized powder, so potential irritation to eyes if in contact with non-diluted product. Not expected to cause serious eye irritation. Not expected to cause eye irritation if reconstituted in solution.
Skin irritation **Skin sensitization**	Not a primary irritant nor primary sensitizer according to results from a human RIPT skin irritation /sensitization study conducted on 50 human subjects (Ref 2).
Further toxicological information	No serious toxicological side effects have been reported during use of this ingredient in skin care products for the last 10 years (Ref 3)

References:

Ref 1: Certificate of Manufacturing for the product BIOEFFECT EGF SERUM.
Ref 2: Report from hRIPT study conducted by AMA Laboratories (MS11.RIPT.L99110.50.CJHI)
Ref 3: QA report Oct 2020: No serious undesirable effects reported on BIOEFFECT products.

12. ECOLOGICAL INFORMATION

Ecotoxicity: No negative harmful effect on the environment if handled and treated in accordance with standard cosmetics industry practices and regulations. Fully biodegradable.
Persistence and degradability: Barley extract that is fully biodegradable.
Other adverse effects: Not studied.

13. DISPOSAL CONSIDERATIONS

Waste treatment method:

Product: Compost in compliance with applicable regulations.
Packaging: Depending of the type of material, in compliance with regulations.

14. TRANSPORT INFORMATION

No special precautions needed in connection with transport
Not a hazardous product

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture: Non-hazardous preparation according to Directive 1999/45/CE and regulation 1272/2008.

Chemical safety assessment: This product is not classified as hazardous substance or mixture according to main regulations.

16. OTHER INFORMATION

Warranty	This MSDS does not replace the technical product file. The above information describes exclusively the safety requirements of the product and is based on our present-day knowledge. Hazards linked to unusual ways of using the product not recommended by the brand and / or the manufacturer have not been evaluated. This data sheet does not replace the user's responsibility to be aware of, to understand and to respect any local, state and/or Federal / National regulations concerning the product's use. All the people in contact with the product have to be informed of relevant exposure controls and personal protection equipment requirements as detailed above.
Disclaimer	For cosmetic applications only. For topical skin applications only.

Hilmar Vidarsson, Regulatory Compliance

ORF GENETICS

ORF Genetics
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Kopavogur, Iceland
Tel: + 354 531 1000
Fax: + 354 531 1001

Pesticide Analyzes Results

02.10.2020

Pesticides Analysis on Barley Seed Extract, freeze-dried powder

Study rationale:
Provisions of Maximum Residue Limits (MRLs) are contained in Regulation (IS) No 672/2008 on maximum levels of pesticides residues in food and feed, incorporated relevant EEA legislation. Analyses of pesticides residues is performed by Matis Laboratories and MAST, the Icelandic Food and Veterinary Authority, is responsible for pesticides residues monitoring programmes in Iceland. To meet MRL standards, on the request of ORF, Matis laboratories have performed pesticides analysis on one production batch of freeze-dried Barley Seed Extracts. Pesticides that were measured were; *Pirimicarb* and *Avemectin.*

Certificate Prepared by:
Hilmar Vidarsson, PhD
Regulatory Compliance Officer

Pesticides Analysis conducted by:
MATIS, a government owned, non-profit, independent research company
Vinlandsleid 12, 113 Reykjavik, Iceland
https://english.matis.is/
Contact: matis@matis.is

Guidelines and methods used for measurements by MATIS, an Accredited laboratory.
Rules on maximum values are according to Regulation no. 672/2008 on pesticide residues in food with subsequent amendments. Sampling and handling according to Regulation 736/2003. The pesticides are extracted by the Quechers method (according to standard EN 15662: 2008) and analysed by gas analyser with mass sensor (GC-MS / MS) and liquid analyser with mass sensor (LC-MS / MS) (Reference for method; T. Pihlström, Method validation and quality control procedures for pesticide residues analysis in food and feed. Document No. SANTE/11945/2015)

Results
MATIS measured *Pirimicarb* and *Avemectin* in one production batch (Lot; DK340) of *Barley Seed Extract* with results as follows *

Samples ID	Date	Samples	Batch (Lot nr)	Pesticides	Concentration (mg/kg)
R17-768-1	22.03.2017	Freeze-dried powder	DK340	avermectin	< LOD
R17-768-1	22.03.2017	Freeze-dried powder	DK340	pirimicarb	< LOD

Conclusion
In brief, pesticides measurements demonstrate that the level of the two pesticides measured, the *Pirimicarb* and *Avermectin*, is below "Level of Detection" (LOD). Hence, this confirms that the levels of pesticides residues in the product of Barley Seed Extracts is way below the MRL levels monitored by MAST, Icelandic Food and Veterinary Authority.

Hilmar Vidarsson, Regulatory Compliance

Results in report "R17-00768-0001**" (see page 2, below and report is available upon request)*

Copy of the report R17-00768-0001, issued by MATIS, an Accredited laboratory

Matís ohf
Vínlandsleið 12
112 Reykjavík
Sími: (354) - 422 5000
Fax: (354) - 422 5001

RANNSÓKNANIÐURSTÖÐUR
Varnarefnamælingar
Útgefnar af faggildri rannsóknarstofu
Report issued by Accredited laboratory

Orf líftækni
Víkurhvarfi 3
203 Kópavogur

Sýni Nr. R17-00768-0001
Varnarefni

Sýnatökudagsetning: 02.03.2017
Móttekið: 03.03.2017
Rannsókn lokið: 22.03.2017

Sýnatökustaður: Orf líftækni, Víkurhvarfi 3, 203 Kópavogur

Sýnatökuaðili: Orf líftækni

Tilefni sýnatöku: Sérstök rannsókn
Sýnatökuseðill nr: ORF-17-1

Skimað fyrir pirimicarb og avermectin

Reglur um hámarksgildi eru skv. Reglugerð nr. 672/2008 um varnarefnaleifar í matvælum með síðari breytingum. Sýnataka og meðhöndlun skv. Reglugerð 736/2003. Varnarefnin eru dregin út með Quechers aðferð (samkvæmt staðli EN 15662:2008) og greind á gasgreini með massaskynjara (GC-MS/MS) og vökvagreini með massaskynjara (LC-MS/MS).

Heimildir aðferðar:
1) T. Pihlström, Method validation and quality control procedures for pesticide residues analysis in food and feed. Document No. SANTE/11945/2015
Mælióvissa efnamælinga byggir á 95% öryggismörkum (k=2).

Niðurstöður varnarefnarannsókna:

Nr. Sýnis	Vörutegund	Varnarefni	Magn mg/kg	Hámark mg/kg**	%***	Óvissa	Lotunr
R17-768-1	Próteinduft	avemectin	<LOD			21%	DK 340
R17-768-1	Próteinduft	pirimicarb	<LOD			20%	DK 340

Einungis þau varnarefni sem mælast eru sýnd í töflu
* Ekki faggildar niðurstöður

Reykjavík 23. mars 2017

Vordís Baldursdóttir
Sérfræðingur

Rafræn undirskrift

Athugasemd: engin

Niðurstöður má eingöngu nota í heild sinni, nema rannsóknarstofan gefi skriflegt leyfi til annars.
Fyrir aftan rannsóknaliði eru aðskenni rannsóknaaðferða og má fá upplýsingar um heimildir þeirra á heimasíðu Matís ohf (www.matis.is)
Niðurstöður gilda aðeins um það/þau sýni sem var/voru rannsakað/rannsökuð.

This is to certify that the skin care product;

BIOEFFECT EGF SERUM
BES001, BES002

which is manufactured and sold by *Bioeffect ehf* located at Vikurhvarf 7, 203-Kopavogur in Iceland, does comply with the regulatory network outlined in the EU Cosmetic Regulation (EC) No. 1223/2009. *Bioeffect ehf* furthermore certifies that this cosmetic product is produced under quality-controlled system and has undergone a safety assessment on the basis of all relevant information in full conformity with the EU regulation, and that the safety report is set up in accordance with Annex I of that regulation.

Composition of BIOEFFECT EGF SERUM:

INCI Name	CAS No.	% INCI	Function
GLYCERIN	56-81-5	]50%-75%]	Humectant /solvent /stabilizer
AQUA	7732-18-5	]25%-50%]	Solvent
SODIUM CHLORIDE	7647-14-5	[0.1%-1%]	Buffering agent
SODIUM HYALURONATE	9067-32-7	[0.1%-1%]	Humectant / skin conditioning
BARLEY SH-OLIGOPEPTIDE-1	1807528-51-3	[0%-0.1%]	Skin conditioning
TROMETHAMINE (Tris)	77-86-1	[0%-0.1%]	Buffering agent
HORDEUM VULGARE SEED EXTRACT	85251-64-5	[0%-0.1%]	Skin conditioning

Bioeffect ehf ensures that all ingredients in the product **BIOEFFECT EGF SERUM** conform to the European regulation for cosmetic products, (EC) No. 1223/2009.

KOPAVOGUR, 29 NOV 2019

Hilmar Viðarsson
Regulatory Compliance

BIOEFFECT EHF
Vikurhvarf 7
Kopavogur, Iceland
Tel: + 354 531 1000
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SKIN SENSITIZATION AND IRRITATION EVALUATION OF BIOEFFECT™ EGF SERUM

contains 0.1% Hordeum Vulgare Seed Extract

HRIPT test conducted by
AMA Laboratories, Inc. NY, USA
April 11, 2011ORF Genetics

Main conclusions:

BIOEFFECT™ EGF Serum may be considered:
NON-PRIMARY IRRITANT to the skin
NON-PRIMARY SENSITIZER to the skin

Study summary:

Objective:
The goal was to assess if BIOEFFECT™ EGF Serum induces contact sensitization and/or irritation by repetitive applications to the skin of healthy human volunteers.

General information:

Service Company:	AMA Laboratories, Inc. NY, USA.
Test:	50 human subjects RIPT skin irritation/sensitization evaluation (Occlusive Patch)
Test Material:	BIOEFFECT EGF SERUM, Lot # DK39
AMA Ref. no.:	MS11.RIPT.L99110.50.CHI
Date:	April 11, 2011
Evaluation period:	From March 7 through April 8, 2011

Summary:

The study was conducted to determine the sensitization and/or irritation potential of BIOEFFECT™ EGF Serum after repeated application under occlusive patches to the skin of human subjects. The study enrolled 53 subjects that applied occlusive patch with BIOEFFECT™ EGF Serum directly on skin for 24 hours. This was repeated until a series of nine consecutive 24 hours exposures had been made, at approximately 48 hours intervals. Of the 53 subjects that started 50 subjects completed the study. Ten to fourteen days after application of the last patch, challenge patch was applied once to previously unexposed site and reactions graded 24 and 48 hours post-application.

Results and conclusions:

Under the exposure conditions described in the test protocol, test material BIOEFFECT™ EGF Serum did not induce any adverse reactions during the course of this study and may therefore be considered a ***NON-PRIMARY IRRITANT*** and a ***NON-PRIMARY SENSITIZER*** to the skin.

References:

AMA Laboratories, INC. test report No. MS11.RIPT.L99110.50.CH (see pages 2 – 11 below)

AMA LABORATORIES, INC.
216 Congers Road, Bldg. 1
New City, NY 10956 USA
(845) 634-4330
FAX: (845) 634-5565
www.amalabs.com

50 HUMAN SUBJECT REPEAT INSULT PATCH TEST SKIN IRRITATION/SENSITIZATION EVALUATION (Occlusive Patch)

AMA Ref. No.: MS11.RIPT.L9911O.50.CHI

Date: April 11, 2011

Sponsor: Centerchem, Inc.
20 Glover Avenue
Norwalk, Connecticut 06850

1.0 Objective:

Consumer products or raw materials designed for consistent reapplication to areas of the skin may, under proper conditions, prove to be contact sensitizers or irritants in certain individuals. It is the intention of a Repeat Insult Patch Test (RIPT) to provide a basis for evaluation of this irritation/sensitization potential if such exists.

2.0 Test Material:

2.1 Test Material Description:

On March 1, 2011 one test sample labeled Bioeffect Serum EGF, Lot # DK39 was received from Centerchem, Inc. and assigned AMA Lab No. L-9911.

2.2 Handling:

Upon arrival at AMA Laboratories, Inc., the test material is assigned a unique laboratory code number and entered into a daily log identifying the lot number, sample description, sponsor, date received and tests requested.

Samples are retained for a period of three months beyond submission of final report unless otherwise specified by the sponsor or, if sample is known to be in support of governmental applications, representative retained samples are kept two years beyond final report submission.

Sample disposition is conducted in compliance with appropriate federal, state and local ordinances.

2.3 Test Material Evaluation Prerequisite:

Prior to induction of a human test panel, toxicology, microbiology or in-vitro performance spectra may be required to assess the feasibility of commencement as dictated by an Institutional Review Board (IRB) described in Section 3.0.

Sponsor purports that prior to sample submission the following tests were conducted with no adverse results and that the test data are on file on their premises and have not been made available to AMA personnel:

- USP or CTFA Preservative Efficacy Test or equivalent
- 90 Day Accelerated Stability and Container Compatibility Study

3.0 Institutional Review Board:

Reference: CFR Title 21 Part 56, Subparts A, B, C, and D. The IRB of AMA Laboratories, Inc., consists of five or more individuals, chosen from within the company for technical expertise and from the local community for lay interaction. The list of IRB members is kept on file at AMA Laboratories, Inc. and is available for inspection during the hours of operation.

4.0 Panel Selection:

4.1 Standards for Inclusion in a Study:

- Individuals who are not currently under a doctor's care.
- Individuals free of any dermatological or systemic disorder which would interfere with the results, at the discretion of the Investigator.
- Individuals free of any acute or chronic disease that might interfere with or increase the risk of study participation.
- Individuals who will complete a preliminary medical history form mandated by AMA Laboratories, Inc. and are in general good health.
- Individuals, who will read, understand and sign an informed consent document relating to the specific type of study they are subscribing. Consent forms are kept on file and are available for examination on the premises of AMA Laboratories, Inc. only.
- Individuals able to cooperate with the Investigator and research staff, willing to have test materials applied according to the protocol, and complete the full course of the study.

4.2 Standards for Exclusion from a Study:

- Individuals under 18 years of age.
- Individuals who are currently under a doctor's care.
- Individuals who are currently taking any medication (topical or systemic) that may mask or interfere with the test results.
- Subjects with a history of any acute or chronic disease that might interfere with or increase the risk associated with study participation.
- Individuals diagnosed with chronic skin allergies.
- Female volunteers who indicate that they are pregnant or lactating.

4.3 Recruitment:

Panel selection is accomplished by advertisements in local periodicals, community bulletin boards, phone solicitation, electronic media or any combination thereof.

4.4 Informed Consent and Medical History Forms:

An informed consent was obtained from each volunteer prior to initiating the study describing reasons for the study, possible adverse effects, associated risks and potential benefits of the treatment and their limits of liability. Panelists signed and dated the informed consent document to indicate their authorization to proceed and acknowledge their understanding of the contents. Each subject was assigned a permanent identification number and completed an extensive medical history form. These forms along with the signed consent forms, are available for inspection on the premises of AMA Laboratories, Inc. only. Reference 21 CFR Ch. 1 Part 50, Subpart B.

The parties agree to comply with applicable state and federal privacy laws for the use and disclosure of a subject's personal health information by taking reasonable steps to protect the confidentiality of this information. This obligation shall survive the termination or expiration of this Agreement.

5.0 Population Demographics:

Number of subjects enrolled		53
Number of subjects completing study		50
Age Range		18-69
Sex	Male	10
	Female	43
Race	Caucasian	46
	Hispanic	6
	Asian	1

6.0 Equipment:

- Patch Description: Parke-Davis Hypoallergenic Readi Bandages or the equivalent.
- 1ml volumetric syringe without a needle.

7.0 Procedure:

- Subjects are requested to bathe or wash as usual before arrival at the facility.
- 0.2 ml or 0.2g of the test material is dispensed onto the occlusive, hypoallergenic patch.
- The patch is then applied directly to the skin of the infrascapular regions of the back, to the right or left of the midline and the subject is dismissed with instructions not to wet or expose the test area to direct sunlight.
- After 24 hours the patch is removed by the panelist at home.
- This procedure is repeated until a series of nine consecutive 24 hour exposures have been made for every Monday, Wednesday, and Friday for three consecutive weeks.
- In the event of an adverse reaction, the area of erythema and edema is measured. The edema is estimated by the evaluation of the skin with respect to the contour of the unaffected normal skin. Reactions are scored just before applications two through nine and the next test date following application nine. In most instances this is approximately 24 hours after patch removal. Clients are notified immediately in the case of adverse reaction and determination is made as to treatment program if necessary.
- Subjects are then given a 10 - 14 day rest period after which a challenge or retest dose is applied once to a previously unexposed test site. The retest dose is equivalent to any one of the original nine exposures. Reactions are scored 24 and 48 hours after application.
- Comparison is made between the nine inductive responses and the retest dose.

8.0 Results:

Please refer to attached Table.

9.0 Observations:

No adverse reactions of any kind were noted during the course of this study.

10.0 Archiving:

All original samples, raw data sheets, technician's notebooks, correspondence files and copies of final reports and remaining specimens are maintained on premises of AMA Laboratories, Inc. in limited access storage files marked "Archive". A duplicate disk copy of final reports is separately archived in a bank safe deposit vault.

11.0 Reference:

Appraisal of the Safety of Chemicals in Food, Drugs and Cosmetics, published by The Association of Food and Drug Officials of The United States, 1965 (modified).

12.0 Security Label Disclosure:

To prevent loss of and protect intellectual property, original, certified documents issued by AMA Laboratories Inc. can be identified by a proprietary, tamper evident security hologram affixed to all Conclusion/Signature pages on final reports. Any attempt to remove the hologram will irreversibly damage the label and leave an immediate trace, thus invalidating the document.

Only reports containing the AMA LABS, INC. hologram will be recognized by AMA Laboratories Inc. as a certified original.

13.0 Conclusions:

The test material (AMA Lab. No.: L-9911; Client No.: Bioeffect Serum EGF, Lot # DK39) when tested under occlusion as described herein, may be considered:
a **NON-PRIMARY IRRITANT** and **NON-PRIMARY SENSITIZER** to the skin according to the reference.

Mayya Tatsene, M.D.
Study Director

Breanna Wanamaker, A.A. (Candidate)
Technician

David R. Winne, B.S.
Technical Director

4/11/11
Date

TABLE
SUMMARY OF RESULTS
(Occlusive Patch)

AMA Lab No.: L-9911
Client No.: Bioeffect Serum EGF, Lot # DK39

No.	Subject ID	RACE	SEX	Response 1	2	3	4	5	6	7	8	9	Chall. 24 HR	Chall. 48 HR	Score
1	34 1401	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
2	36 7970	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
3	36 8248	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
4	36 8618	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
5	38 2191	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
6	38 7929	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
7	44 1289	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
8	44 7613	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
9	46 0816	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
10	48 3564	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
11	48 4304	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
12	50 2448	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
13	50 7349	C	F	0	0	0	0	0	0	Dc	Dc	Dc	Dc	Dc	N/A
14	50 9982	H	F	0	0	0	0	0	0	0	0	0	0	0	0.0
15	52 3942	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
16	54 3415	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
17	54 7235	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
18	54 7647	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
19	54 7891	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
20	56 0908	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
21	56 1816	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
22	56 3465	H	F	0	0	0	0	0	0	0	0	0	0	0	0.0
23	60 3986	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
24	60 4534	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
25	60 5842	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
26	62 0840	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
27	62 2960	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
28	62 9835	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
29	64 5526	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0

AMA Lab No.: L-9911
Client No.: Bioeffect Serum EGF, Lot # DK39

No.	Subject ID	RACE	SEX	Response 1	2	3	4	5	6	7	8	9	Chall. 24 HR.	48 HR.	Score
30	64 6740	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
31	64 8133	H	F	0	0	0	0	0	0	0	0	0	0	0	0.0
32	66 1649	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
33	68 8375	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
34	70 3684	C	M	0	0	Dc	Dc	Dc	Dc	Dc	Dc	Dc	Dc	Dc	N/A
35	72 3555	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
36	74 1855	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
37	76 0933	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
38	76 1298	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
39	76 8279	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
40	76 8434	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
41	78 7400	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
42	78 8079	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
43	80 1611	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
44	80 4126	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
45	82 0569	H	F	0	0	0	0	0	0	0	0	0	0	0	0.0
46	82 0760	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
47	82 6224	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
48	82 6807	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
49	84 2189	C	M	0	0	0	0	0	0	0	0	0	0	0	0.0
50	87 6602	H	F	0	0	0	0	Dc	Dc	Dc	Dc	Dc	Dc	Dc	N/A
51	88 4232	C	F	0	0	0	0	0	0	0	0	0	0	0	0.0
52	90 6566	H	F	0	0	0	0	0	0	0	0	0	0	0	0.0
53	96 0145	A	M	0	0	0	0	0	0	0	0	0	0	0	0.0

Evaluation Period:

This study was conducted from March 7, 2011 through April 8, 2011.

Scoring Scale and Definition of Symbols Shown in Table:

0 - No evidence of any effect

? - (Barely perceptible) minimal faint (light pink) uniform or spotty erythema

1 - (Mild) pink uniform erythema covering most of contact site

2 - (Moderate) pink\red erythema visibly uniform in entire contact area

3 - (Marked) bright red erythema with accompanying edema, petechiae or papules

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

D - Patch eliminated due to reaction

Dc - Discontinued due to absence of subject on application date

M - Patch applied to an adjacent site after strong test reaction

N/A - Score is not calculated for subjects discontinued before challenge

S - Skin stained from pigment in product

T - Tan

NOTE: All technical employees of AMA LABORATORIES, INC. are required to take and pass a visual discrimination examination conducted by a Board Certified Ophthalmologist using the Farnsworth-Munsell 100 Hue Test as published; which determines a person's ability to discern color against a black background. This test was additionally modified to include a flesh tone background more nearly approaching actual use conditions, wherein erythematous skin is graded according to intensity.

14.0 Quality Assurance Statement:

This study was inspected in accordance with the Standard Operating Procedures of AMA Laboratories, Inc. To assure compliance with the study protocol, the Quality Assurance Unit completed an audit of the study records and report.

Report reviewed by:

Kamil Wojtowicz

Kamil Wojtowicz, M.S.
Quality Assurance Supervisor

4/11/11
Date

BIOEFFECT

BIOEFFECT EHF
Vikurhvarf 7
203 Kopavogur
Iceland

1.10.2020

QA report Oct2020; No undesirable effects reported on BIOEFFECT products

Operation under QMS system:

BIOEFFECT EHF., operates according to a Quality Management System (QMS) which is based on the following:

1. Regulation (EC) No 1223/2009 of the European Parliament and of the Council of 30 November 2009 on cosmetic products
2. ISO-9001:2008 Quality management system – Requirements
3. ISO-22716 Cosmetics – Good Manufacturing Practices (GMP) – Guidelines on Good Manufacturing Practices

BIOEFFECTs QMS is certified by an accredited certification body.

As a part of biannual reports, a summary is made of complaints received by BIOEFFECTs headquarters. Complaints are classified according to type of complaint. Type C-complaints concern customers reactions on their skin

Results of annual reports on C-complaints:

There have been no serious undesirable effects reported for any of the BIOEFFECT products containing the ingredient ***Barley Seed Extract***. These products have been sold in more than one million (**> 1.000.000**) units over a period of 10 years. Only limited number of complaints, or notifications have been reported during this time. The percentage of these minor complaints has been only **~ 0.005%** of sold units. This is a very low ration of unwanted skin reaction complaints, of which the most frequently reported effects have been a mild irritation, itching and small pimples, all of which are classified as minor or mild.

Date of Issue: 1.10.2020

On behalf of BIOEFFECT,

Sigríður Hjörleifsdóttir

Sigríður Hjörleifsdóttir
Quality Manager

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: October 6, 2020

SUBJECT: Products Containing 0.005% Hordeum Vulgare Extract

Consumer Product Testing Co. 2015. Ophthalmological in-use safety evaluation - 50% sensitive eyes (eye cream containing 0.005% Hordeum Vulgare Extract).

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

Consumer Product Testing Co. 2017. Repeated insult patch test (pressed powder containing 0.005% Hordeum Vulgare Extract).

Ager. 2016. Human primary skin irritation test (product containing 0.005% Hordeum Vulgare Extract).

Consumer Product Testing Co.

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Ophthalmological In-Use Safety Evaluation - 50% Sensitive Eyes. Protocol No.: [redacted]

TEST MATERIAL: Eye Cream - [redacted]

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: [redacted]

Approved by: [redacted]

Approved by: [redacted]

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

[redacted]

QUALITY ASSURANCE UNIT STATEMENT

Trial Number: [redacted]

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

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

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

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

[redacted] [redacted]

Quality Assurance Representative Date

[redacted]

Objective: To evaluate the safety and ocular irritation potential of an eye cream following repetitive, daily use conditions.

Participants: Thirty-two female subjects, ages 20 to 64 years, were recruited and qualified for this trial. Twenty-seven subjects completed the trial. Subject #'s 5, 11, 26, 27 and 30 did not complete the trial due to personal reasons unrelated to test material use.

Inclusion Criteria:

a. Approximately 30 healthy female subjects, ages 18 to 65 years, inclusive;
b. Approximately 50% of the panel had self-perceived sensitive eyes;
c. Subjects who agreed to discontinue use of their current product with similar function and use only the test material;
d. Approximately 50% of the panel were soft contact lens wearers;
e. Subjects who agreed to arrive at the Testing Facility without eye makeup;
f. Subjects who were regular users of a product with similar function;
g. Subjects who agreed to avoid introducing the use of any new cosmetic, toiletry or personal care product during the course of the trial;
h. Subjects who had an acceptable ophthalmic examination to ensure eye health and, if appropriate, the correct fit and condition of their contact lenses;
i. Subjects who read, understood and signed an Informed Consent Form that included a HIPAA statement; and
j. Subjects who were considered dependable and able to follow directions as outlined in the protocol.

Exclusion Criteria:

a. Subjects in ill health or taking medication, other than birth control, which could have influenced the purpose, integrity or outcome of the trial;
b. Subjects who were currently using any systemic or topical corticosteroids, anti-inflammatory drugs, antihistamines or retinoids or other medication that, in the opinion of the Investigator, may have influenced the outcome of the trial;
c. Females who were pregnant, nursing or planning on becoming pregnant during the course of the trial;
d. Subjects who had a history of adverse reactions to similar products being tested; or
e. Subjects with any visible skin or eye disease that might have been confused with a reaction to the test material.

Test Material: Eye Cream - [redacted]

[redacted]

Trial Schedule:

Initiation Date	Completion Date
March 13, 2015	April 10, 2015

Methodology:

Each subject received a qualifying ophthalmic examination by a Board Certified Ophthalmologist to ensure eye health and, if appropriate, the correct fit of their contact lenses.

The Ophthalmologist studied and evaluated by gross and/or slit lamp examination the subjects' eyelids, conjunctivae, corneas, irises, lenses, anterior chambers and pupillary reactions, in addition to measuring visual acuity.

Findings were noted on subjects' Ocular Case Report Forms.

The panel was comprised of 15 soft contact lens wearers. The remaining subjects were non-contact lens wearers. In addition, 15 subjects reported self-perceived sensitive eyes.

After completion of the ophthalmic examination, qualified subjects received the test material and were instructed to use the test material at least once a day for 4 weeks, according to the following directions:

Instructions:

Discontinue the use of your current eye cream and use only the test material provided for the duration of this trial. You are permitted to use your own makeup products for the duration of this trial. Do not introduce any new cleansing products, moisturizers or other cosmetics during the trial interval.

Do not wear eye makeup on examination days.

Contact wearers, please wear your contacts on examination days.

Usage Directions:

Gently apply a small amount with fingertip under and around the eye area in the morning and evening.

Applications must be recorded on the daily diary.

Keep out of reach of children. Do not let anyone else use the test material

[redacted]

Methodology (continued):

Report any adverse reactions or problems immediately to the Testing Facility staff.

To document compliance, subjects were required to maintain a daily diary to record each use.

A comprehensive ocular examination, as previously described, was conducted for each subject after 4 weeks of test material usage.

All unused test material and daily diaries were returned to the Testing Facility at the final visit.

Daily diaries were reviewed for completeness, prior to dismissal of the subjects.

Amendments: There were no amendments.

Deviations: There were no deviations.

Adverse Events: There were no adverse events.

Results: All ophthalmologic examinations remained within normal limits throughout the test interval.

Subject demographics are presented in Table 1.

All ophthalmological examination Case Report Forms and daily diaries are provided under separate cover.

Summary: Under the conditions of this trial, test material, Eye Cream - [redacted] did not indicate a potential for ophthalmologic irritation. This test material can be considered safe for use by both contact and non-contact lens wearers, as well as individuals with normal or self-perceived sensitive eyes.

[redacted]

Table 1

Subject Demographics

Subject Number	Initials	Age	Contact Lens	Eye Sensitivity
1	C-S	57	Non	No
2	KRJ	48	Non	Yes
3	JCG	36	Non	No
4	MNE	61	Non	No
5	SPP	31	Soft	Yes
6	SLD	52	Non	No
7	T-Z	51	Non	Yes
8	DBP	59	Non	Yes
9	GBD	23	Soft	Yes
10	A-B	51	Non	Yes
11	M-R	49	Non	Yes
12	JMD	23	Soft	Yes
13	S-H	29	Soft	Yes
14	M-P	20	Non	Yes
15	EBL	52	Soft	Yes
16	SMM	51	Soft	No
17	JCF	48	Soft	No
18	MLP	26	Non	Yes
19	A-M	61	Soft	No
20	WAM	46	Soft	Yes
21	EAA	52	Soft	No
22	DML	49	Soft	No
23	MSL	45	Soft	No
24	HND	64	Non	No
25	LMP	29	Non	No
26	R-C	44	Non	No
27	MBI	24	Soft	No
28	SLS	51	Soft	Yes
29	CIC	44	Soft	No
30	JCD	29	Non	No
31	VCT	49	Non	No
32	TLV	53	Non	Yes

Did Not Complete: Subject #'s 5, 11, 26, 27 and 30

[redacted]

Consumer Product Testing Co.
TST 1975

FINAL REPORT

CLIENT: [redacted]

ATTENTION: [redacted]

TEST: Repeated Insult Patch Test
Protocol No.: [redacted]

TEST MATERIAL: Face Mask [redacted]

EXPERIMENT REFERENCE NUMBER: [redacted]

Reviewed by: [redacted]

Approved by: [redacted]

Approved by: [redacted]

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

Consumer Product Testing Co.
ESTABLISHED 1975

QUALITY ASSURANCE UNIT STATEMENT

Study Number: C16-0735.01

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

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

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

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

[redacted]

04-13-2016
Date

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

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

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

Inclusion Criteria:

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

Exclusion Criteria:

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

Test Material: Face Mask [redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
[redacted]	February 22, 2016	March 31, 2016
	February 24, 2016	March 31, 2016

[a]With parental or guardian consent

Methodology:

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

Induction Phase:

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

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

Rest periods consisted of one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

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

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

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

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

Adverse Events:

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

Amendments:

There were no amendments.

Deviations:

There were no deviations.

Results:

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

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary:

Under the conditions of this study, test material, Face Mask - [redacted] indicated no potential for dermal irritation or allergic contact sensitization.

[redacted]

Table 1
Panel [redacted]

Individual Results

Face Mask [redacted]

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

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

[redacted]

Table 1
(continued)
Panel [redacted]

Individual Results

Face Mask - [redacted]

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

Day 1* = Supervised removal

Table 1
(continued)
Panel #[redacted]

Individual Results

Face Mask -[redacted]

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

Day 1* = Supervised removal

Table 1
(continued)
Panel [redacted]

Individual Results

Face Mask [redacted]

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

Day 1* = Supervised removal

Table 2
Panel [redacted]

Subject Demographics

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

Table 2
(continued)
Panel [redacted]

Subject Demographics

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

Table 2
(continued)
Panel [redacted]

Subject Demographics

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

Table 2
(continued)
Panel [redacted]

Subject Demographics

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

Consumer Product Testing Co

FINAL REPORT

CLIENT:

ATTENTION:

TEST: Repeated Insult Patch Test
Protocol No.:

TEST MATERIAL: PRESSED POWDER-

EXPERIMENT REFERENCE NUMBER:

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

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

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

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

Consumer Product Testing Co

QUALITY ASSURANCE UNIT STATEMENT

Study Numbe[redacted]

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

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

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

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

[redacted]

Quality Assurance Representative

Date

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

Participants: One-hundred seventeen (117) qualified subjects, male and female, ranging in age from 22 to 70 years, were selected for this evaluation. One-hundred seven (107) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

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

Exclusion Criteria:

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

Test Material: PRESSED POWDER– [redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
[redacted]	July 24, 2017	September 1, 2017

[a]With parental or guardian consent

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

Participants: One-hundred seventeen (117) qualified subjects, male and female, ranging in age from 22 to 70 years, were selected for this evaluation. One-hundred seven (107) subjects completed this study. The remaining subjects discontinued their participation for various reasons, none of which were related to the application of the test material.

Inclusion Criteria:

a. Male and female subjects, age 16[a] to 79 years.
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Exclusion Criteria:

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

Test Material: PRESSED POWDER–[redacted]

Study Schedule:

Panel #	Initiation Date	Completion Date
[redacted]	July 24, 2017	September 1, 2017

[a]With parental or guardian consent

Methodology:

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

Induction Phase:

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

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

Rest periods consisted of one day following each Tuesday and Thursday removal, and two days following each Saturday removal.

Challenge Phase:

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

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

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

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

Adverse Events: There were no adverse events.

Amendments: There were no amendments.

Deviations: Subject #71 was given entry into the clinical trial despite having insufficient rest from the previous patch trial. The subject's patches were removed within 30 minutes of application and the subject was removed from the trial by the Principal Investigator. The Principal Investigator judged this deviation to have no influence on clinical trial results.

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

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary: Under the conditions of this study, test material, PRESSED POWDER–[redacted] indicated no potential for dermal irritation or allergic contact sensitization.

Methodology (continued):

Evaluation Criteria (Erythema and additional Dermal Sequelae):

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

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

Adverse Events: There were no adverse events.

Amendments: There were no amendments.

Deviations: Subject #71 was given entry into the clinical trial despite having insufficient rest from the previous patch trial. The subject's patches were removed within 30 minutes of application and the subject was removed from the trial by the Principal Investigator. The Principal Investigator judged this deviation to have no influence on clinical trial results.

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

Observations remained negative throughout the test interval.

Subject demographics are presented in Table 2.

Summary: Under the conditions of this study, test material, PRESSED POWDER– [redacted] indicated no potential for dermal irritation or allergic contact sensitization.

Table 1

Panel [redacted]

Individual Results

PRESSED POWDER– [redacted]

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

Day 1* = Supervised removal

Table 1
(continued)
Panel [redacted]
Individual Results

PRESSED POWDER– [redacted]

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

Day 1* = Supervised removal
m = Additional makeup day granted at the discretion of the clinic supervisor
DNC = Did not complete study

Table 1
(continued)
Panel # [redacted]

Individual Results

PRESSED POWDER– [redacted]

Subject Number	Induction Phase									Virgin Challenge Site	
	Day1*	1	2	3	4	5	6	7	8	9	Day1*	Day 3
59	0	0	0	0	0	0	0	0	0	0	0	0
60	0	0	0	0	0	0	0	0	0	0	0	0
61	0	0	0	0	0	0	0	0	0	0	0	0
62	0	0	0	0	0	0	0	0	0	0	0	0
63	0	0	0	0	0	0	0	0	0	0	0	0
64	0	0	0	0	0	0	0	0	0	0	0	0
65	0	0	0	0	0	0	0	0	0	0	0	0
66	0	0	0	0	0	0	0	0	0	0	0	0
67	0	0	0	0	0	0	0	0	0	0	0	0
68	0	0	0	0	0	0	0	0	0	0	0	0
69	0	0	0	0	0	0	0	0	0	0	0	0
70	0	0	0	0	0	0	0	0	0	0	0	0
71	----------DID NOT COMPLETE STUDY----------											
72	0	0	0	0	0	0	0	0	0	0	0	0
73	0	0	0	0	0	0	0	0	0	0	0	0
74	0	0	0	0	0	0	0	0	0	0	0	0
75	0	0	0	0	0	0	0	0	0	0	0	0
76	0	0	0	0	0	0	0	0	0	0	0	0
77	0	0	0	0	0	0	0	0	0	0	0	0
78	0	0	0	0	0	0	0	0	0	0	0	0
79	0	0	0	0	0	0	0	0	0	0	0	0
80	0	0	0	0	0	0	0	0	0	0	0	0
81	0	0	0	0	0	0	0	0	0	0	0	0
82	0	0	0	0	0	0	0	0	0	0	0	0
83	0	0	0	0	0	0	0	0	0	0	0	0
84	0	0	0	0	0	0	0	0	0	0	0	0
85	0	0	0	0	0	0	0	0	0	0	0	0
86	0	0	0	0	0	0	0	0	0	0	0	0
87	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal

Table 1
(continued)
Panel #[redacted]

Individual Results

PRESSED POWDER–[redacted]

Subject Number	Day1*	Induction Phase 1	2	3	4	5	6	7	8	9	Virgin Challenge Site Day1*	Day 3
88	0	0	0	0	0	0	0	0	0	0	0	0
89	0	0	0	0	0	0	0	0	0	0	0	0
90	0	0	0	0	0	0	0	0	0	0	0	0
91	0	0	0	0	0	0	0	0	0	0	0	0
92	0	0	0	0	0	0	0	0	0	0	0	0
93	0	0	0	0	0	0	0	0	0	0	0	0
94	0	0	0	0	0	0	0	0	0	0	0	0
95	0	0	0	0	0	0	0	0	0	0	0	0
96	0	0	0	0[m]	0	0	0	0	0	0	0	0
97	0	0	0	0	0	0	0	0	0	0	0	0
98	0	0	0	0	0	0	0	0	0	0	0	0
99	----------DID NOT COMPLETE STUDY----------											
100	0	0	0	0	0	0	0	0	0	0	0	0
101	0	0	0	0	0	0	0	0	0	0	0	0
102	0	0	0	0	0	0	0	0	0	0	0	0
103	0	0	0	0	0	0	0	0	0	0	0	0
104	0	0	0	0	0	0	0	0	0	0	0	0
105	0	0	0	0	0	0	0	0	0	0	0	0
106	0†	----------DID NOT COMPLETE STUDY----------										
107	0	0	0	0	0	0	0	0	0[m]	0	0	0
108	0	0	0	0	0	0	0	0	0	0	0	0
109	0	0	0	0	0	0	0	0	0	0	0	0
110	0	0	0	0	0	0	0	0	0	0	0	0
111	0	0	0	0	0	0	0	0	0	0	0	0
112	0	0	0	0	0	0	0	0	0	0	0	0
113	0	0	0	0	0	0	0	0	0	0	0	0
114	0	0	0	0	0	0	0	0	0	0	0	0
115	0	0	0	0	0	0	0	0	0	0	0	0
116	0	0	0	0	0	0	0	0	0	0	0	0
117	0	0	0	0	0	0	0	0	0	0	0	0

Day 1* = Supervised removal
m = Additional makeup day granted at the discretion of the clinic supervisor
† = Unsupervised removal

Table 2

Panel [redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
1	RNC	54	F
2	EWB	45	M
3	CES	48	F
4	A-C	44	F
5	CEC	51	F
6	M-A	70	F
7	BCP	22	F
8	J-A	24	M
9	QAT	37	M
10	PVM	52	F
11	PAS	51	F
12	MDT	33	F
13	PRG	32	M
14	GPR	51	F
15	MAR	67	M
16	PMD	52	F
17	L-T	69	F
18	DLP	60	M
19	RMS	66	F
20	DLM	61	F
21	M-B	46	F
22	JOJ	55	M
23	MDD	53	F
24	M-G	62	F
25	L-P	52	F
26	LDW	64	F
27	C-K	62	F
28	D-W	36	F
29	MDJ	51	F

Table 2
(continued)
Panel [redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
30	WJS	52	F
31	KMG	52	F
32	JLM	50	F
33	M-R	44	F
34	GPM	26	F
35	LDB	68	F
36	D-R	40	F
37	LGP	22	F
38	EJS	41	F
39	SSP	22	F
40	MBS	60	F
41	G-O	57	F
42	LJF	57	F
43	HMT	60	M
44	EDT	58	F
45	RIT	54	F
46	G-C	60	F
47	E-A	43	F
48	PRK	61	M
49	M-P	57	F
50	NAL	32	F
51	XLO	55	F
52	AYC	38	M
53	LIG	61	F
54	IRV	62	F
55	LCC	34	F
56	IST	27	M
57	DFM	48	M
58	KJT	29	F

Table 2
(continued)
Panel #[redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
59	GAF	68	F
60	NMG	51	F
61	CLR	43	F
62	CHW	55	F
63	REC	69	F
64	EJZ	42	F
65	IXM	22	F
66	MJS	48	F
67	DAS	53	M
68	DEK	61	F
69	MBL	36	F
70	BCS	49	F
71	A-E	29	F
72	J-V	24	M
73	J-S	67	M
74	M-S	67	F
75	DAP	47	F
76	DET	58	F
77	WPM	39	M
78	JMG	43	F
79	AAF	48	M
80	SDW	47	F
81	J-O	45	F
82	PLY	67	F
83	TEC	53	F
84	TMM	35	F
85	L-K	64	F
86	LCK	39	F
87	DML	52	F

Table 2
(continued)
Panel [redacted]

Subject Demographics

Subject Number	Initials	Age	Gender
88	JCS	52	F
89	MRM	43	F
90	MAL	37	F
91	CJP	55	M
92	SAR	34	F
93	LAM	47	F
94	DLM	63	F
95	ORP	29	M
96	EMV	56	F
97	SAD	38	F
98	HJR	45	M
99	NLT	70	F
100	LIM	42	F
101	WJM	65	M
102	KJP	37	F
103	C-P	40	F
104	JMM	24	F
105	DLC	51	F
106	DAH	39	F
107	LMA	42	F
108	MLT	35	F
109	S-D	44	M
110	LAC	56	F
111	K-M	63	F
112	DLM	47	F
113	ETT	51	M
114	F-W	60	M
115	L-D	59	M
116	TJE	57	M
117	R-E	48	F

AGER

Ager lab Test procedure I

SAGGIO DI IRRITAZIONE CUTANEA PRIMARIA SU UOMO
HUMAN PRIMARY SKIN IRRITATION TEST

Numero di studio / *Study number*: Data / *Date*: 10.06.2016

CLIENTE / *SPONSOR*:

PRODOTTO / *PRODUCT:*
Nome o descrizione / *Name or description*: **POWDER PP**
Codice o numero di catalogo / *Code or catalogue number*:
Codice AGER identificativo del controcampione / *AGER identification code of the test sample*: A0597/16
Prot. n. / *Prot. n.*: 21/16 - 4

COORDINAZIONE DEL SAGGIO / *ASSAY COORDINATION*:
Organizzazione / *Organization*:

Direttore dello studio / *Study director*:

ESECUZIONE DEL SAGGIO / *ASSAY PERFORMANCE*:
Sede delle prove / *Testing facility*:

Dermatologo / *Dermatologist*:

METODO / *METHOD*: La procedura è descritta in dettaglio nella Metodica Ager, MT03.
/ *The procedure is described in the Ager Test Procedure MT03.*

RISULTATI / *RESULTS*: I risultati sono descritti nelle tabelle compilate dal responsabile della Sperimentazione clinica Dermatologica, dr.ssa E.C. Schmitt, delle quali si allega fotocopia. I risultati contenuti nel presente rapporto riguardano unicamente il campione esaminato. / *Results are shown in the attached tables, signed by the supervisor Dr. E.C. Schmitt, Dermatologist responsible for the Investigation. The results presented in this final report concern only the sample tested.*

COMMENTO / *COMMENT*: Il prodotto in esame, applicato tal quale in condizioni occlusive sulla cute sana del dorso di 20 volontari, ha dato indice di irritazione medio pari a **0,10** dopo 15 min., ed a **0,05** dopo 24 ore dalla rimozione del campione. In base alla scala utilizzata, il prodotto può pertanto essere classificato come *non irritante* e probabilmente innocuo se applicato sulla cute umana. / *The test product, applied undiluted under occlusive conditions onto intact back skin of 20 healthy volunteers, has shown an average irritation index of **0,10** 15 min. and **0,05** 24 hours after patch removal. According to the adopted classification, the product can be considered non-irritant and probably safe when applied on human skin.*

Direttore dello studio / *Study director*

AGER srl – 20900 Monza (MB) – Via Santuario delle Grazie Vecchie, 1 – Tel. +39-039.2326260 – Fax +39-039.328342 – E-mail: info@ager.it – Web: www.ager.it
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Prot. n.: / *Prot. n.:*	21/16 - 4	Numero di studio: / *Study number:*	;	Data: / *Date:*	10.06.2016

RISULTATI DEL TEST DI IRRITAZIONE CUTANEA SULL'UOMO
RESULTS OF HUMAN PRIMARY SKIN IRRITATION TEST
(Patch test a 48 ore / *48 hours Patch test*)

PRODOTTO / *PRODUCT:*

Vol n.	Sesso/ *Sex*	ERITEMA/ *ERYTHEMA*		EDEMA/ *OEDEMA*		ALTRO/*OTHER* Vescicolazione/*Vescicles*	
		15min.	24h	15min.	24h	15min.	24h
1	F	0	0	0	0	0	0
2	F	**1**	**1**	0	0	0	0
3	F	0	0	0	0	0	0
4	F	0	0	0	0	0	0
5	F	0	0	0	0	0	0
6	F	0	0	0	0	0	0
7	F	0	0	0	0	0	0
8	F	0	0	0	0	0	0
9	F	0	0	0	0	0	0
10	F	0	0	0	0	0	0
11	F	0	0	0	0	0	0
12	F	0	0	0	0	0	0
13	F	0	0	0	0	0	0
14	F	0	0	0	0	0	0
15	F	0	0	0	0	0	0
16	F	0	0	0	0	0	0
17	F	0	0	0	0	0	0
18	F	**1**	0	0	0	0	0
19	F	0	0	0	0	0	0
20	F	0	0	0	0	0	0

Medico Dermatologo / *Dermatologist*:

AGER

Prot. n.: / *Prot. n.:*	21/16 - 4	Numero di studio: / *Study number:*	Data: / *Date:*	10.06.2016

RISULTATI DEL TEST DI IRRITAZIONE CUTANEA SULL'UOMO
RESULTS OF HUMAN PRIMARY SKIN IRRITATION TEST
(Patch test a 48 ore / *48 hours Patch test*)

PRODOTTO / ***PRODUCT:***

CALCOLO DEI RISULTATI / *CALCULATION OF RESULTS:*

In base ai punteggi individuali riassunti nella tabella, il risultato del saggio di irritazione cutanea primaria può essere così espresso: / *On the basis of the individual scores above indicated the result of human primary skin irritation test may be expressed as:*

INDICE MEDIO DI IRRITAZIONE / ***AVERAGE IRRITATION INDEX:***

15 min.: **0,10** 24h: **0,05**

Medico Dermatologo / *Dermatologist*:

AGER

Prot. n.: *Prot. n.:*	21/16 - 4	Numero di studio: *Study number:*		ata: *Date:*	10.06.2016

RISULTATI DEL TEST DI IRRITAZIONE CUTANEA SULL'UOMO
RESULTS OF HUMAN PRIMARY SKIN IRRITATION TEST
(Patch test a 48 ore / *48 hours Patch test*)

PRODOTTO / *PRODUCT:*

RIASSUNTO DELLA METODICA / *SUMMARY OF THE METHOD:*

Il prodotto è stato applicato tal quale in condizioni occlusive per 48 ore sul dorso di 20 volontari sani.
La lettura delle reazioni cutanee è stata eseguita dopo 15 min. e dopo 24 ore dalla rimozione del prodotto (48 e 72 ore dalla applicazione dello stesso, rispettivamente). /
The produ) was applied undiluted under occlusive conditions for 48 hours onto intact back skin of 20 healthy volunteers. The reading of skin reactions was performed after 15 minutes and after 24 hours from product removal (48 and 72 hours from product application).

ANNOTAZIONI PARTICOLARI / *SPECIFIC REMARKS:*

Segni di reazione allergica sono stati notati in 0 (zero) volontari. / *Signs of allergic reactions were observed in 0 (zero) volunteers.*

COMMENTO / *COMMENT*:

Nelle condizioni sperimentali adottate, il prodotto sopra indicato ha dato INDICE DI IRRITAZIONE a 15 min. pari a **0,10** ed a 24 ore pari a **0,05**. Esso può essere pertanto considerato non irritante e probabilmente innocuo se applicato sulla cute umana. /
*In the experimental conditions adopted the test product showed an AVERAGE IRRITATION INDEX of **0,10** 15 min. and **0,05** 24 hours after patch removal. According to the adopted classification, the product can be considered non-irritant and probably safe when applied on human skin.*

Medico Dermatologo / *Dermatologist*:

Concentration of Use by FDA Product Category – Barley Additions*

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

Ingredient	Product Category	Maximum Concentration of Use
Hordeum Distichon (Barley) Extract	Eye lotions	0.005%
Hordeum Distichon (Barley) Extract	Mascaras	0.3%
Hordeum Distichon (Barley) Extract	Makeup bases	0.1%
Hordeum Distichon (Barley) Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.1%
Hordeum Distichon (Barley) Extract	Face and neck products Not spray	0.005%
Hordeum Distichon (Barley) Extract	Moisturizing products Not spray	1.8%
Hordeum Distichon (Barley) Extract	Night creams, lotions and powders Not spray	0.005%

*Ingredients found only in the title of the table were included in the concentration of use survey, but no uses were reported.

Information collected in 2020
Table prepared: August 11, 2020