Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics

Status:	Draft Final 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. Previous Panel member involved in this assessment: James G. Marks, Jr., M.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, CIR
Date: November 13, 2020
Subject: Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics

Enclosed is the Draft Final Report of the Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics. (It is identified as *wheat122020rep* in the pdf document.)

In June 2020, the Panel reviewed the safety of the 27 ingredients in this report and issued a Tentative Report with the conclusion that the available data are insufficient to make a determination of safety under the intended conditions of use in cosmetic formulations. The Panel's needs were:

- Method of manufacturing data
- Dermal irritation and sensitization data at a test concentration of 13% for Triticum Vulgare (Wheat) Sprout Extract

Since the June Panel meeting, CIR staff have received method of manufacturing data on Triticum Vulgare (Wheat) Germ Extract (*wheat122020data1*), and a technical data sheet and a summary of a single insult patch test on a mixture containing approximately 5% Triticum Vulgare (Wheat) Gluten and sodium laureth sulfate (*wheat122020data2*). These data, and additional information from published literature on wheat allergy, have been incorporated into this draft. These data are highlighted to aid in the Panel's review.

Comments provided by the Council on the Tentative Report have been addressed (*wheat122020pcpc*). Other supporting documents for this report package include a flow chart (*wheat122020flow*), the reports previously published by the Panel (*wheat122020_flour_orig, wheat122020_gluten_glycerides_orig, wheat122020RR*), report history (*wheat122020hist*), transcripts from the previous meeting (*wheat122020min*), a search strategy (*wheat122020strat*), and 2020 VCRP data (*wheat122020fda*).

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

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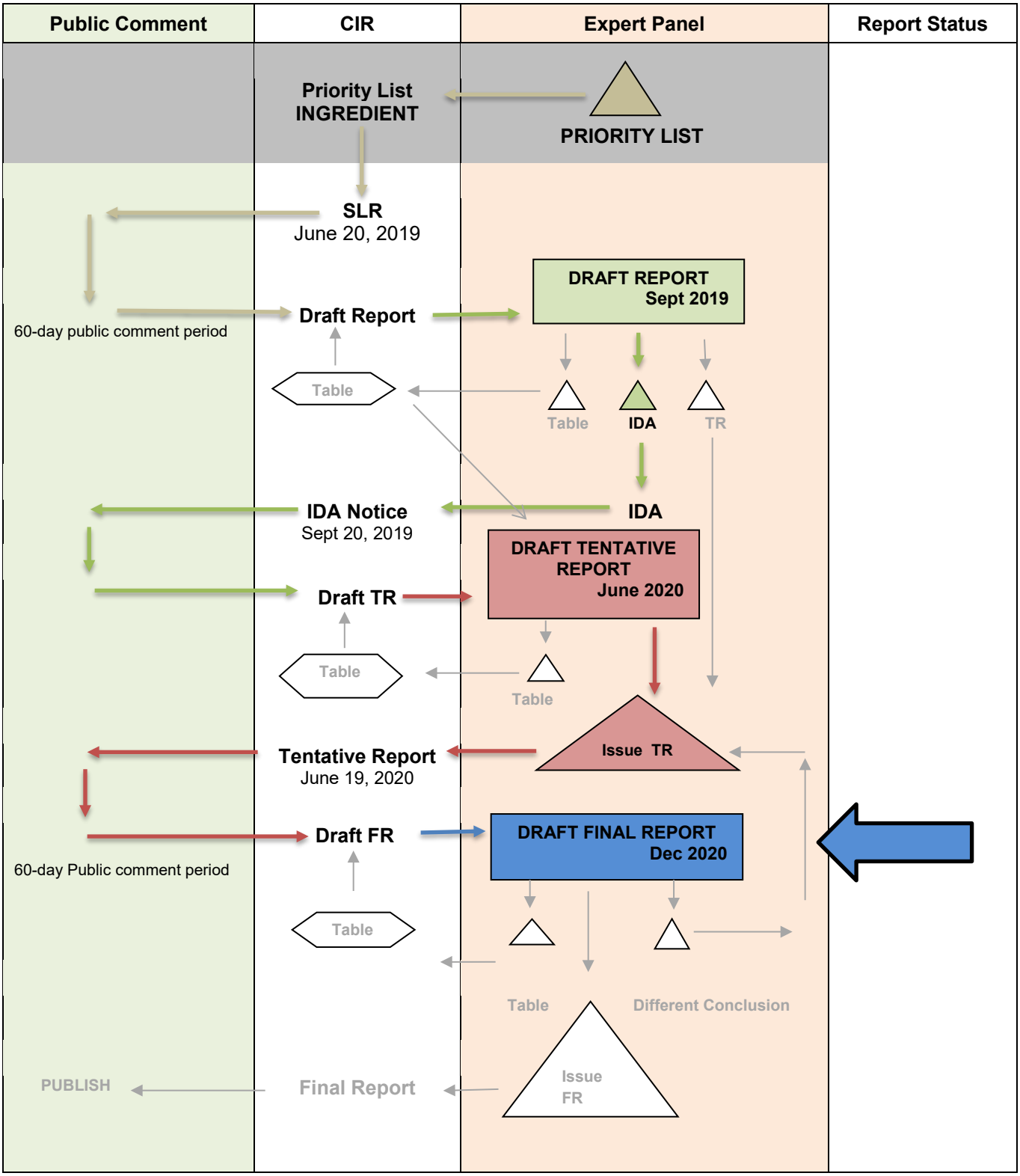
SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Wheat-derived Ingredients

MEETING December 2020



Wheat-derived ingredients History

June 19, 2019 – Scientific Literature Review announced.

September 2019 - the Panel issued an Insufficient Data Announcement. The Panel's needs were:

- Method of manufacturing, composition, and impurities data for Triticum Aestivum (Wheat) Germ Extract, Triticum Aestivum (Wheat) Seed Extract, Triticum Monococcum (Wheat) Seed Extract, Triticum Turgidum Durum (Wheat) Seed Extract, Triticum Vulgare (Wheat) Germ Extract, Triticum Vulgare (Wheat) Seed Extract, and Triticum Vulgare (Wheat) Sprout Extract
- Dermal irritation and sensitization data at maximum leave-on use concentrations for Triticum Aestivum (Wheat) Germ Extract, Triticum Vulgare (Wheat) Germ Extract, Triticum Vulgare (Wheat) Sprout Extract, and Wheat Germ Glycerides

June 2020 – The Panel issued a Tentative Report with the conclusion that the available data are insufficient to make a determination of safety under the intended conditions of use in cosmetic formulations. The Panel's needs were:

- Method of manufacturing data
- Dermal irritation and sensitization data at a test concentration of 13% for Triticum Vulgare (Wheat) Sprout Extract

Wheat-Derived Ingredients, December 2020 – Christina Burnett

						Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irr.			Dermal Sens.				Ocular Irr.		Clinical Studies	
	Reported Use	GRAS	Method of Mfg	Constituents	Impurities	Dermal Penetration	ADME	Dermal	Oral	Inhalation	Dermal	Oral	Inhalation	Dermal	Oral	In Vitro	In Vivo	Dermal	Oral	In Vitro	Animal	Human	In Vitro	Animal	Human	Phototoxicity	In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Triticum Aestivum (Wheat) Flour Lipids	X																												
Triticum Vulgare (Wheat) Flour Lipids	X																												
Triticum Aestivum (Wheat) Germ Extract	X																												
Triticum Vulgare (Wheat) Germ Extract	X		X		X																X				X			X		
Triticum Aestivum (Wheat) Seed Extract	X																												
Triticum Vulgare (Wheat) Seed Extract	X																												
Triticum Aestivum (Wheat) Leaf Extract				X																									
Triticum Aestivum (Wheat) Peptide																													
Triticum Monococcum (Wheat) Seed Extract	X																												
Triticum Monococcum (Wheat) Stem Water																													
Triticum Spelta Seed Water																													
Triticum Turgidum Durum (Wheat) Seed Extract																													
Triticum Vulgare/Aestivum (Wheat) Grain Extract				X	X																								
Triticum Vulgare (Wheat) Bran	X																		X										
Triticum Vulgare (Wheat) Bran Extract	X		X	X												X													
Triticum Vulgare (Wheat) Bran Lipids	X																												
Triticum Vulgare (Wheat) Flour Extract	X			X																									
Triticum Vulgare (Wheat) Germ	X		X	X																									
Triticum Vulgare (Wheat) Germ Powder																													
Triticum Vulgare (Wheat) Germ Protein	X																												

Wheat-Derived Ingredients, December 2020 – Christina Burnett

	Reported Use	GRAS	Method of Mfg	Constituents	Impurities	Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irr.			Dermal Sens.			Phototoxicity	Ocular Irr.		Clinical Studies	
						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		In Vitro	Animal	Retrospective/ Multicenter	Case Reports
Triticum Vulgare (Wheat) Gluten	X *	X	*	X	X																	X			*			*		
Triticum Vulgare (Wheat) Gluten Extract	X																													
Triticum Vulgare (Wheat) Kernel Flour	X		X	X	X																									
Triticum Vulgare (Wheat) Protein	X			X																										
Triticum Vulgare (Wheat) Sprout Extract	X			X											X	X	X		X											
Triticum Vulgare (Wheat) Straw Water																														
Wheat Germ Glycerides	X *		*	*												X					*			*	*			*		
Generic wheat nomenclature																														

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

"*" indicates that data were available in a previous review.

Wheat-Derived Ingredients

Ingredient	CAS #	InfoB	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Triticum Vulgare (Wheat) Germ Extract	84012-44-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Aestivum (Wheat) Flour Lipids		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Aestivum (Wheat) Germ Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Aestivum Leaf Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Aestivum (Wheat) Peptide		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Aestivum (Wheat) Seed Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Monococcum (Wheat) Seed Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Monococcum (Wheat) Stem Water		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Turgidum Durum (Wheat) Seed Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare/Aestivum (Wheat) Grain Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Bran		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Bran Extract	84012-44-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Flour Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Ingredient	CAS #	InfoB	PubMed	TOXNET	FDA	EU	ECHA	IUCLID	SIDS	ECETOC	HPVIS	NICNAS	NTIS	NTP	WHO	FAO	NIOSH	FEMA	Web
Triticum Vulgare (Wheat) Flour Lipids		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Germ		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Germ Powder		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Germ Protein		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Protein		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Seed Extract	84012-44-2	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Sprout Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Straw Water		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Spelta Seed Water		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Bran Lipids		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Kernel Flour		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Gluten	8002-80-0	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Triticum Vulgare (Wheat) Gluten Extract		√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√
Wheat Germ Glycerides	68990-07-8	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√	√

Botanical and/or Fragrance Websites (if applicable)

Ingredient	CAS #	Dr. Duke's	Taxonomy	GRIN	Sigma-Aldrich	AHPA	EMA	AGRICOLA	SSA	IFRA	RIFM
Triticum Vulgare (generic)		√	√	√	√	√	√	√	X		
Tritium Aestivum (generic)		√	√	√	√	√	√	√	X		

Search Strategy

PubMed

Triticum Vulgare Germ Extract (NOT fermented) – 189 hits, 2 relevant
Triticum Aestivum Flour Lipids (NOT bread, NOT pasta, NOT noodles) – 199 hits, 3 relevant
Triticum Aestivum Germ Extract – SAME AS TRITICUM VULGARE EXTRACT
Triticum Aestivum Leaf Extract – 61 hits, 3 relevant
Triticum Aestivum Peptide – 2354 hits; limited search to toxicity - 126 hits, 3 relevant
Triticum Aestivum Seed Extract – 176 hits, 4 relevant
Triticum Monococcum Seed Extract – 0 hits
Triticum Monococcum Stem Water – 0 hits
Triticum Spelta Seed Water – 745 hits; limited search to toxicity – 59 hits, 0 relevant
Triticum Turgidum Durum Seed Extract – 9 hits, 1 relevant
Triticum Vulgare/Aestivum Grain Extract – 16 hits, 2 relevant
Triticum Vulgare Bran – 835 hits; limited search to toxicity – 21 hits, 2 relevant
Triticum Vulgare Bran Extract – 39 hits, 1 relevant
Triticum Vulgare Bran Lipids – 193 hits, 0 relevant
Triticum Vulgare Flour Extract – 104 hits, 4 relevant
Triticum Vulgare Flour Lipids – 299 hits, 5 relevant
Triticum Vulgare Germ – 1785 hits; limited search to toxicity – 21 hits, 1 relevant
Triticum Vulgare Germ Powder – 9 hits, 1 relevant
Triticum Vulgare Germ Protein – 1308 hits; limited search to toxicity – 16 hits, 1 relevant
Triticum Vulgare Kernel Flour (2000-2019) – 62 hits, 1 relevant
Triticum Vulgare Gluten (2000-2019) – 2943 hits; limed search to toxicity NOT dietary NOT celiac – 13 hits, 1 relevant
Triticum Vulgare Gluten Extract – 91 hits, 0 relevant
Triticum Vulgare Protein – 12,306 hits; limited search to toxicity – 422 hits, 4 relevant
Triticum Vulgare Seed Extract – SAME AS TRITICUM AESTIVUM SEED EXTRACT
Triticum Vulgare Sprout Extract – 11 hits, 7 relevant
Triticum Vulgare Straw Water – 343 hits, 0 relevant
Wheat Germ Glycerides (2000-2019) – 7 hits, 0 relevant

Search updated October 2020.
Search for "wheat induced respiratory allergy NOT WDEIA" = 57 returns, 10 retrieved.

LINKS

Search Engines

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

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

Pertinent Websites

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

Botanical Websites, if applicable

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

SEPTEMBER 2019 PANEL MEETING – INITIAL REVIEW/DRAFT REPORT

Belsito's Team Meeting – September 16, 2019

DR. BELSITO: Wheat. So this is the first time we're looking at these wheat-derived ingredients. Wheat. So I guess the first question I had out to all of you, particularly to Dan, are we mixing too many different chemical classes here -- carbohydrates, proteins, fat, nonabsorbable fibers?

DR. LIEBLER: I don't think so. The main ingredients, obviously wheat germ extract, and that contains all of those anyway. So these are all subsets of the main ingredient which has a very good data package. So I don't have any problem with any of them.

DR. BELSITO: Okay. I guess when -- just on page 13, one, two, three -- it says, most of the ingredients reviewed in the safety assessment may be consumed as food. So we're just assuming things like flour extract or wheat flour and bran extract is bran and sprout -- wheat sprouts?

MS. BURNETT: I believe that's wheatgrass.

DR. BELSITO: That's?

MS. BURNETT: Wheatgrass. People drink that -- those shots at the juice bars.

DR. BELSITO: Okay. But people vape there too. Okay. So, in terms of the inhalation here, is this a potential issue for gluten-sensitive people?

DR. SNYDER: Kind of one of my questions is there's a gluten protein and nongluten protein, so I assume so. I mean, some of the most severe reactions people can have are from inhaling firewood that's got poison ivy on it and burning it and inhaling the smoke. So I would think inhalation would be --

DR. KLAASSEN: But it is a GI phenomenon.

DR. BELSITO: Right.

DR. KLAASSEN: I don't know.

DR. BELSITO: And then we don't really have good composition data.

DR. SNYDER: I thought we did. My comment was lots of impurities and constituent data.

DR. BELSITO: No, when I got to dermal sensitization, I said, insufficient for all except glycerides and germ extract unless composition data is essentially the same.

DR. SNYDER: Table 3 is four different bran extracts.

DR. BELSITO: Yeah that's wheat bran extracts. That's it.

DR. LIEBLER: That really doesn't tell you too much.

DR. BELSITO: What?

DR. LIEBLER: I said, that really doesn't tell you too much.

DR. BELSITO: Yeah. We don't have any.

DR. LIEBLER: The text, though, actually has a lot of description that is not in tables, so the text under composition impurities Page 15. It's fairly extensive and seems reasonably redundant too. It's the kinds of things

that you would expect to be in botanicals, grains. Not only do they mention the usual sort of innocuous fatty acids and lipids and so on -- other lipids -- but they also do cite abundances of some sterols, phytosterols, flavonoids.

And these are across wheat germ, wheat flour extract, wheat grain extract. Even the leaf extract is mentioned, although I think it's the leaf is a little thin on method of manufacture as is the straw water. Those are the two that I thought were inadequate.

But there is, for example, at the bottom of page 15, just one example here. Wheat sprout extract. Hydroalcoholic extract was determined to be composed of -- and the text just listed in general terms or provides the citation. I don't know, for example, in Reference 24, I didn't look at that; whether or not that contains a table of data or some other data that could be excerpted into tables. I mean, some of the stuff on this page could be probably put into a table that would better lay out the similarities and give us a better picture of what the supporting data are with these.

I think where we're a little thin on method of manufacture is just what are representative methods to produce these different subgroups, like the bran lipids, the flour lipids. In general, we know how lipid extracts are made, so we wouldn't need a lot. But it would be good if we could have a couple of those. But things like the straw water and the leaf extract aren't described. These are also ingredients that aren't used, so probably nobody's doing it.

DR. EISENMANN: By definition, the water is a distillation product.

DR. LIEBLER: It's not defined in the document.

DR. EISENMANN: I mean, I'm just saying that's how water is -- ingredients that are named waters are supposed to all be distillation products.

DR. LIEBLER: Right, but we just don't have anything.

DR. EISENMANN: Okay.

DR. BELSITO: On PDF page 19, the HRIPT on the human, the way it's worded it appears like the material was applied just as a single patch, and so it'd just be an irritation assay. Test material was applied as supplied. The patches were partially occluded, no irritation or sensitization. There were no further details. I mean, I presume that they removed it after 24 hours. There were three patches per week. It was done for three weeks. They rested for two weeks.

Because when we're looking at this, we need to look at the quality of the study and there's really no -- you can't even say OECD guidelines because it really doesn't exist for HRIPT. At least when you say that, if there are no further details, we assume that it was done according to those guidelines.

MS. BURNETT: The full study starts on PDF page 77. I can add more details to that.

DR. BELSITO: Yeah, so that is what was done. You can just see it in the table -- Week 1, Week 2, Week 3, Week 4, Week 5 and 6 and 7. Well, yeah, I think with ones that we can say it was done according to a certain guideline that the details of the study should be in there.

DR. LIEBLER: Carol, I do see what you're referring to in Table 1 of the definitions -- when you said, by definition, I understand now, for the straw water, for example.

DR. BELSITO: So you're okay with not having a composition on that?

DR. LIEBLER: I think we have enough information to continue, yeah.

DR. BELSITO: Okay. So we have sensitization and irritation data only on the glyceride and the germ extract. Is that sufficient to carry the rest?

DR. LIEBLER: I think the germ extract should have most of the ingredients, most of the chemical components. The glyceride would not. so that's not representative of the more complex ingredients. But the germ extracts should contain most of the ingredients. And it really depends on exactly how the extracts are prepared.

DR. BELSITO: I sort of thought Table 3 was misleading because it really doesn't tell us the composition of the bran extract. It tells us all the other stuff that's in there depending upon how it's extracted. But it tells us the impurities that can be found in bran extract depending upon the method of extraction, right? I mean there's not a single detail about what is bran extract.

DR. LIEBLER: Given that wheat germ extract and wheat seed extract have the greatest number of uses, we don't have any real information about their method of manufacture. And I do think that's an insufficiency in this report. Not that I really have a concern about them, but there's no description of how they're produced. The way the extracts were produced would certainly influence the components that would be present particularly because of constituents of concern for sensitization.

DR. BELSITO: Okay. I thought it was insufficient as well, but I have many more issues than you in terms of composition. But you're comfortable with composition. You want insufficient for manufacturing?

DR. LIEBLER: For wheat germ extract, wheat seed extract, those are the two major ones.

DR. BELSITO: Of wheat germ?

DR. LIEBLER: And wheat seed extracts.

DR. BELSITO: Just method of manufacture and impurities, obviously.

DR. LIEBLER: Right. I think we actually have more composition data than it looks like from tables because the text actually refers to a lot of information that could be probably put in the tables.

DR. SNYDER: We have this old wheat flour and starch report which has a ton of composition data in it. There must be 30 references here, abundant literature containing chemical/physical characteristics of wheat flour and its components. And it'll be the same for wheat starch. It's on page 45 of that old CR report.

DR. BELSITO: What page is that?

DR. SNYDER: Page 45 of the PDF, chemical/physical properties for wheat flour, wheat starch. I mean, we know there's constituents of concern, so we're going to deal with that with our statement, right?

DR. BELSITO: But that won't give us information on the germ extract and the seed extract. Will it?

DR. SNYDER: I don't know. I didn't get to know what composes the flour as far as the --

DR. BELSITO: Well, the flour must be different than the seed extract and the germ extract. I mean, what's the definition here in this current --

DR. SNYDER: Yeah, the bran extract, the germ extract, the seed extract.

DR. LIEBLER: The flour contains everything, I think, except the bran components, right?

DR. BELSITO: Right.

DR. SNYDER: Okay.

DR. LIEBLER: Take off the bran and then you mill it. And you don't extract out, so you've got everything still in the flour. The extracts are subsets of the flour; at least the wheat germ extract would be a subset of the flour. And,

depending on how it's extracted, you can get different collections of chemicals. Seed extract, I presume, includes the bran as well. Is that right?

DR. BELSITO: I would think that seed extract would be the seed you put in the ground to get the wheat to grow, no?

DR. KLAASSEN: That's the same as what you eat, isn't it?

DR. SNYDER: I think we need a botany lesson here.

DR. BELSITO: Let's go back to Christina's definitions.

DR. KLAASSEN: I kind of think the flour is everything also.

MS. BURNETT: When I was reading it, I was getting that the kernel flour and the flour flour and the seed were all the same thing. But it's hard to tell sometimes from the botanical descriptions in how they mesh with the INCI nomenclature definitions.

DR. BELSITO: It says the bran is the outer layer of the grain formed by the fused fruit and seed wall in grains and cereals. The endosperm is the energy storage area within the seed, so the endosperm is in the seed. The germ is the embryo in the seed, so it's in the seed. The grain is dry seed. The kernel is the grain;, so it doesn't sound like there's a difference between kernel and grain.

DR. SNYDER: I think it's all in the flour. Whatever the flour has, it’s everything.

DR. KLAASSEN: I think so too.

DR. BELSITO: Pericarp is the front fruit wall. The seed is, I presume, the grain.

DR. LIEBLER: The seed encompasses all of it -- the bran and the germ.

MS. BURNETT: I have on here, it says, the dried fruit of the wheat plant may be referred to as seed, grain or kernel.

DR. BELSITO: The sprout is the seedling. It's a young little grain, a young little wheat.

DR. SNYDER: I don't see any reason to believe that everything is not within the flower. These are all just subdivisions of what constitutes the flower.

DR. BELSITO: You're from the Midwest, Curt.

DR. KLAASSEN: Yeah, I've never raised wheat. But that's my interpretation too. If you have the wheat seed or the wheat flour that's the whole thing, of the grain that is.

MS. BURNETT: Because I have drawings and no two drawings labeled it the same.

DR. BELSITO: Yeah, correct.

DR. LIEBLER: There are similarities.

DR. SNYDER: I think from a plant standpoint, that we have plenty constituent data until we get to when it becomes extracted; because of what Dan said, and then they have different chemicals and you can do an ethanol extraction. You can do a --

DR. LIEBLER: Ethanol water. You can do just an aqueous extracts.

DR. SNYDER: Based on that, then we may need some data to understand what kind of ingredients or chemicals may be left over from that extraction method. Is that what you were saying?

DR. LIEBLER: Yeah. I mean, I think that we're -- if there are a lot of producers, there are probably going to be a lot of variations on the basic methods. These are probably mainly aqueous extracts or a little bit hydroalcoholic extracts. And if we can get a method of manufacture on the wheat germ extract and the wheat seed extract, that's going to pretty much cover -- it would be representative enough to cover everything. The wheat seed extract covers the bran as well as the germ. The wheat germ is the middle part of the inside of the seed; and that would cover all the extracts.

MS. BURNETT: In a similar vein for the pomegranate report that we issued the IDA back in April, we asked for a method of manufacturing for the extracts, especially with regard to the solvent type used. So we can use a similar language.

DR. SNYDER: Yeah.

DR. BELSITO: So we're going for insufficient for manufacture and impurities of the extracts.

DR. LIEBLER: Yes.

DR. BELSITO: That would be just the seed and the germ as you previously asked for or the leaf extract, all of the extracts?

DR. LIEBLER: We could ask for them all; but I think we could end up using the seed and the germ extracts to clear everything.

DR. SNYDER: To cover more than one, yeah.

DR. LIEBLER: I think that's a reasonable inference. That won't get us the leaf and it won't get us the straw water compositions.

DR. BELSITO: Okay. But are we now asking for all or simply saying the germ and the seed will cover everything?

DR. LIEBLER: The germ and the seed will cover. So, if we ask for those, I think we've got a reasonable chance for getting that.

DR. BELSITO: So manufacturing and impurities of the germ extract and the seed extract.

DR. LIEBLER: Right.

DR. BELSITO: And where are we on the fact that we just have sensitization for glyceride and germ extract?

DR. LIEBLER: Well, I think the glyceride only covers the glyceride; whereas the germ extract could cover a lot of the other ingredients.

DR. BELSITO: So you think that we don't need additional sensitization and irritation, you can read across from the germ extract?

DR. LIEBLER: Right.

DR. BELSITO: Okay.

DR. LIEBLER: I think we could. Another thing that occurs to me is that page that does have the composition information and a lot of text, I think it's PDF 13.

MS. BURNETT: Um hmm.

DR. LIEBLER: If in those references there's description of how the extracts will be prepare that gave rise to those chemical inventories; if that information could be put into the table along with what was in there, that would provide weight of evidence for us to associate the kinds of ingredients with the types of preparations. Even if we end up getting limited information on the actual cosmetic ingredient, wheat germ extract for example.

DR. BELSITO: Okay. In the discussion, we obviously have the plant boilerplate with the aflatoxins for this one. How are we going to handle inhalation since that boilerplate is not done yet? And then the gluten issue, which I agree with Curt, that's more of a GI ingestion.

DR. SNYDER: We do have -- I marked it. Look, there are eighteen uses with ingestion potential for the germ extract and there's a bran extract with .015 percent with ten uses with ingestion potential.

DR. BELSITO: Okay.

DR. SNYDER: So we do have -- there's not a -- I think there is a --

DR. KLAASSEN: But again the amount is minimal compared to eating a piece of bread. Actually, I found something on the internet that's kind of interesting. It says that the bran is the hard, outer shell which is made up mostly of fiber. The germ is the nutrient-rich embryo that would sprout into a new plant. And the endosperm is the largest part of the grain which is mostly starch. Whatever.

DR. LIEBLER: So that is consistent with the seed containing all of those things and the bran and the germ described as you indicate. But if we had method of manufacture for the seed extract and the germ extract, I think we'd be in pretty good shape for composition and impurities too.

DR. BELSITO: Okay. So, I guess, back to my question, Bart, how are we going to handle the respiratory as we try to refine the boilerplate, acknowledging WVE's concerns?

DR. HELDRETH: Maybe one of these instances where it's more of something we have to look at on a case-by-case basis. I mean, we have boilerplate's that are not really applicable. And if we don't have the information to clear the inhalation safety, then maybe that's an insufficiency.

DR. LIEBLER: So this is the first time we're seeing this report, right?

DR. BELSITO: Right.

DR. HELDRETH: Yes.

DR. LIEBLER: And I don't know how far people feel that we are on the inhalation, and I don't want to open that discussion right now, but it might be that that inhalation boilerplate is ready for us to use in time for us to craft the right discussion in the next iteration of this report.

DR. BELSITO: So stay where we are right now?

DR. LIEBLER: Yeah. I think maybe we can note that we -- I hadn't really been thinking about the inhalation on this. I guess it was brought up in the WVE -- was that in the WVE?

MS. BURNETT: It was on Silica.

DR. BELSITO: No, that was --

DR. LIEBLER: Oh silica. Okay.

DR. BELSITO: Yeah.

DR. HELDRETH: The place that this report is in the process, of course, as a draft report. In all likelihood it sounds like this team is looking to go towards an insufficient data announcement. But then, after the insufficient data announcement comment period runs out, then it will be up to Christina to provide you with a draft discussion. So any information you can help give her whether it be for inhalation or plant boilerplate.

DR. BELSITO: That's why I'm saying it now. And then the other thing is what we just discussed about gluten and products that they could be ingested.

DR. SNYDER: I mean, we have a category of the wheat gluten, and there's no uses that have a potential for ingestion. There are other wheat components that have ingestion potential. But there's none for the wheat gluten; but if we just kept that in the discussion maybe.

DR. BELSITO: Okay.

DR. HELDRETH: Previously, the Panel has concluded on two gluten ingredients, the gluten hydrolyzed wheat and set a molecular weight limit.

DR. SNYDER: For 3500, yeah.

DR. HELDRETH: Based on the epitope size per IgE.

DR. BELSITO: But that was based on IgE-mediated allergy. The gluten allergy is more skin Dermatitis Herpetiformis with absorption and celiac disease. So it's a different type of reactivity.

DR. LIEBLER: Is there any literature basis for concern about the respiratory allergy to wheat?

DR. BELSITO: No. I mean I think that it's dust. Like, you know, with the cotton people.

DR. LIEBLER: Right.

MS. BURNETT: What I saw talked about the allergies would be like from whatever weeds were mixed in with the wheat. And possibly aflatoxins. So it would be contaminates more than it would be the wheat itself.

DR. BELSITO: Yeah.

DR. LIEBLER: Okay. I was just wondering if I missed something. So we don't have anything on it.

DR. BELSITO: Otherwise, a wheat-allergic person couldn't survive in the middle of Kansas.

DR. KLAASSEN: Fortunately, we didn't live in the center of Kansas.

DR. SNYDER: It says here gluten has to get to the GI tract to cause a reaction called celiac disease. Inhaling is one route through which gluten could potentially be ingested.

DR. BELSITO: Really. Where'd you get that?

DR. SNYDER: Right here on the National Celiac Association website.

DR. BELSITO: Wow.

DR. SNYDER: If you are exposed to airborne flour, it is a potential -- it will get to the nose, the mouth and throat and get swallowed down the GI tract.

DR. BELSITO: Yeah, but is it in any powder? Is there any significant --

DR. KLAASSEN: That might be if you work in an elevator.

DR. SNYDER: Well, I think it's, again, it's that cumulative effect. So if you're getting a little bit through inhalation and you get a little bit -- you know what I mean?

DR. LIEBLER: So there you're surrounded by wheat particles. And indeed breathing those -- if there's any possible respiratory allergy from that, that's the maximum exposure situation possible.

Here, aside from this 13 percent face powder, I think it was, which is sort of an outlier, all of these concentrations are really low as Kurt just pointed out. And that's not necessarily the entire answer, but that's a big part, I think, of our discussion. It's certainly a discussion point when we handle this.

DR. SNYDER: There's another site here that says that inhaling can be enough to trigger celiac disease symptoms. Evidence that airborne gluten --

DR. LIEBLER: Causing the GI symptoms though, right?

DR. SNYDER: Yeah.

DR. HELDRETH: Page 19 does have some occupational exposures to it. It probably represents a much worse exposure scenario than could be possibly in cosmetics.

DR. LIEBLER: I wonder if any of those cited publications references 48 to 50 in the bakery workers. That talks about IgE-mediated wheat flour sensitization. I wonder if there's any reference to any respiratory in that literature or whether --

DR. KLAASSEN: It does say symptoms typically include rhinitis and asthma and other respiratory symptoms.

DR. LIEBLER: Oh, there it is.

DR. KLAASSEN: I guess what we should do is indicate that this is a possibility. We don't have great data, but we kind of later on try and explain it, our relative lack of concern.

DR. BELSITO: Well, the exposures are low. I mean, I've raised this before on medications. Like we have some steroids for use in the scalp that are in peanut oil and others. Now, theoretically, the peanut oil should not contain protein, and we'll actually get to that with an ingredient that we're going to look at that has peanutamide or something in it; I forget what. Where the EU limits the amount of protein contaminant in the oil. I don't think we have any basis in science to do that. And in fact, medications in the US, that's not done either. There's simply a warning; you know, caution, this contains peanut oil that could potentially be contaminated with peanut protein causing reactions. I mean, there's no mechanism for that in cosmetics to have a warning label like that?

MS. BURNETT: I mean, I've seen this. It's not mandatory. If something has wheat, though, they might spell it out, caution, this product might contain wheat. But I think it's -- more on the converse side, I've seen the label say that this product does not contain parabens gluten.

DR. BELSITO: Oh, well, that's feeding to consumer paranoia. Paraben-free, fragrance-free, phthalate-free.

MS. BURNETT: I've seen wheat-free. But I don't think there's -- there's no labeling requirements. If you have that allergy, you would have to read the label to know about it.

DR. SNYDER: I know people who have peanut and gluten, and they're pretty good at reading labels.

DR. BELSITO: Mm-hmm.

DR. KLAASSEN: There's supposedly a new drug or something that's come out to treat peanut allergies. I wonder what that is. This was last week.

DR. LIEBLER: It's a peanut extract.

DR. KLAASSEN: Is it?

DR. LIEBLER: Yeah.

DR. KLAASSEN: So how -- what's going on? How's it working?

DR. LIEBLER: They're just trying to desensitize.

DR. KLAASSEN: Oh, it's a desensitization.

DR. LIEBLER: It's a peanut extract, and I think it's $2400 a dose, so go figure.

DR. BELSITO: Expensive peanut.

DR. LIEBLER: This hasn't even been approved by the FDA. It's only been a report of an expert committee that examined it. I don't think the FDA's taken any action on it yet.

DR. BELSITO: Actually, in Israel they just came with a great study for the common foods that cause allergies. They just feed the babies with them early, and they've noted a reduction.

MS. BURNETT: I'm just thinking as a mother, like, they told you until like -- for certain things, don't feed them anything until they're at least a year. Now, they're going backward.

DR. BELSITO: And they're doing just the opposite.

DR. KLAASSEN: Now, they're saying just the opposite.

DR. BELSITO: Give it to them.

DR. KLAASSEN: That's why there's so many kids with allergies today. There were no such things when I was a kid.

MS. BURNETT: You weren't supposed to give the like eggs, and milk, and all the main things until they were at least a year.

DR. BELSITO: Right.

DR. KLAASSEN: You have to be careful what these physicians tell you what to do and not do.

DR. BELSITO: We're getting off-topic. Let's get back to how we deal with wheat allergy here in the discussion for Christina. We simply say the concentrations are such that we don't think it's an issue. But what is the basis for making that statement?

DR. LIEBLER: I think we would say that if we knew that the incidence of respiratory allergy to wheat is low. Now, if you were a respiratory doc, you would be able to say, in my practice, I very seldom see it. Like you often say in skin, we just never see this clinically. But we need to hit the literature a little bit more to make that determination, I think.

MS. BURNETT: You want to look at those references from the occupational?

DR. LIEBLER: Yeah.

MS. BURNETT: Okay.

DR. LIEBLER: I think it would be a good idea to look at those occupational exposure references.

DR. BELSITO: But occupational would self-select. It's always an issue when you're looking at any kind of occupational data; if you have an issue, you leave that occupation.

DR. LIEBLER: It's quite possible. I mean, you're right. On the other hand, that's better than not having anything. And I think that we needn't necessarily be limited to these three papers on occupational exposures. For example, in your literature search, Christina, do you explicitly look for respiratory, allergy and the ingredients?

MS. BURNETT: Not explicitly.

DR. LIEBLER: If it comes up, it comes up, but you don't go after it. So I think until Christina's had a chance to search for any literature on this, we're just speculating.

DR. KLAASSEN: Yeah.

DR. BELSITO: Okay. I have a reference here. It says that -- a couple of references basically. Studies utilizing food challenge method of diagnosis estimated wheat allergy of prevalence of .1 to .6 in Europe. However, in the US wheat is reported as one of eight most common IgA-mediated food allergens.

A recent study indicated a world-wide prevalence of .5 to 9 percent. And a recent study .4 percent of US adults reported an allergy to wheat. It's highest amongst children and most children "grow out of it" and resolve over time.

DR. LIEBLER: Is any of that explicitly respiratory?

DR. BELSITO: Well there's another one. Let me go back. This was just looking at "wheat allergy." There's one that says, fewer cases of -- in the US, the instance of celiac disease and the wheat allergies estimated to lie around one percent of the population. There's been a 6.4 percent increase in case reports of celiac disease between 1990 and 2009. It's the hypoglycemia of the 2000s. Everyone has it, maybe not. And the incidence of wheat allergy per se, not celiac, has stayed around the same.

DR. SNYDER: They have it -- in that old report there's quite a bit of sensitization data. There's the wheat germ glyceride, patch tested up to 2 percent; 11 hundred subjects, wheat -- gluten patch tested one percent.

DR. LIEBLER: That's what we have in this report, those two.

DR. BELSITO: Those two things?

DR. LIEBLER: Yeah.

DR. KLAASSEN: Here's on the internet, wheat allergy is an allergic reaction to foods containing wheat. Allergic reactions can be caused by eating wheat but also, in some cases, by inhaling wheat flour.

And then it goes on to say that wheat allergy is sometimes confused with celiac disease, but these conditions differ. A wheat allergy occurs when your body produces antibodies to proteins found in wheat. And celiac disease, a specific protein in wheat, gluten, causes a different kind of abnormal immune system response. So it apparently can be two different things.

DR. BELSITO: So probably the best paper, Christina, is there's one from *Clinical Experimental Gastroenterology* in 2014: US perspective on gluten-related diseases. And it's more of a review. Let me see if I can download it.

DR. LIEBLER: So all this stuff seems to filter down to the gut and focus on gut allergy as opposed to respiratory. We were talking about respiratory. I don't think we have any problems having supporting data on gut allergy and what to do with that. The question I think was respiratory.

DR. BELSITO: Right.

DR. LIEBLER: And I think we can't really discuss it until we know if there are data out there; and we are going to need to give Christina time to look.

DR. KLAASSEN: I agree. I think we need to have some more data on this to have a little bit more confidence.

DR. BELSITO: Your email isn't popping up for me, Christina.

MS. BURNETT: Oh, I'll send it to you?

DR. BELSITO: What is your email?

MS. BURNETT: [email address provided]

DR. BELSITO: Two Ts, right?

MS. BURNETT: Yes. Did you get the one I just sent you?

DR. BELSITO: No, I'll send you that paper now.

MS. BURNETT: You're still at Vanderbilt?

DR. LIEBLER: I have both, yeah. I'll look and see when it was sent.

DR. BELSITO: Then we're suggesting what for Christina to look up.

DR. LIEBLER: Respiratory, allergy from wheat.

DR. BELSITO: Okay. What I have is insufficient for manufacturing and impurities of germ extract and wheat seed extract. And any that -- so we think sensitization will cover -- or once we have those rather, that will cover -- the sensitization data that we have for the glyceride and germ extract will cover those, right?

DR. LIEBLER: Yeah. I think particular the germ extract. But that's another reason why I'd like to have some more representative information on how the germ extracts are produced.

DR. BELSITO: And then, in the discussion, we're doing the usual botanical boilerplate. We're still trying to figure out the respiratory boilerplate. Christina's going to do a little bit. I just sent -- I think it's pretty good in terms of epidemiologic data on incidence of wheat allergy and gluten sensitivity in the US population.

MS. BURNETT: Got it.

DR. BELSITO: But you'll just need to figure out reports of airborne wheat allergy, whether they exist.

DR. LIEBLER: Right. Yeah, I think that's really important for us here.

DR. BELSITO: Which one is used up to 30 percent? It's the flour.

DR. LIEBLER: Thirteen.

DR. BELSITO: Thirteen percent. It's the flour?

DR. LIEBLER: Yeah, I think it's in the face powder.

DR. SNYDER: Face powder. Thirteen percent, .6 percent highest for the rest.

DR. BELSITO: So, yeah. We definitely should.

DR. SNYDER: Yeah.

DR. BELSITO: Because to get an allergic reaction you don't need to get the particles down into the alveoli, you just need to get it into the upper respiratory tract.

Okay, so we need to add a little bit about the epidemiology of wheat allergy in the US, and incidence of airborne wheat reactions, someplace in the document so that we can bring them into the discussion. Is that correct?

DR. LIEBLER: Correct.

DR. BELSITO: Okay. Anything else on this report?

DR. LIEBLER: No. Overall, it's really quite good.

Marks' Team Minutes – September 16, 2019

DR. MARKS: Thank you. The first set of ingredients are the wheat ingredients. This is the first review of these 24 ingredients, three of which were previously reviewed, the vulgare kernel flower, the vulgare gluten, and the wheat germ glycerides were found to be safe.

There are three species of wheat in these 24 ingredients. There are multiple plant parts, and there are a number of extracts: germ, leaf, seed, bran, flower, gluten, sprout. There have been some occupational Type 1 reactions reported -- skin and respiratory.

And you may recall that previously we reviewed hydrolyzed wheat protein and gluten in limited molecular weight because of Type 1 sensitivity that had been caused by soaps containing these ingredients in Japan, I believe. So, first, Ron and Tom, any need to reduce the 27 ingredients or change them?

DR. SLAGA: I didn't have any deletions.

DR. SHANK: I have that we have HRIPTs at use concentrations or above for Triticum vulgare germ extract, Triticum vulgare gluten and wheat germ glycerides.

DR. MARKS: Yep.

DR. SHANK: All the rest are insufficient, needing skin sensitization.

DR. MARKS: Any other needs?

DR. SHANK: No.

DR. BERGFELD: Can I ask for clarification? We discussed this last ingredient, one of the last -- only one of these is a GRAS, but they talk about food additives throughout. So how are we considering this?

DR. SHANK: Let me find the list.

DR. MARKS: And I'm going to go back to your HRIPTs, Ron, in a minute because I want to be clear.

DR. SHANK: Okay.

DR. MARKS: I have a little different take. Let's first clarify -- because, again, we could do a table like Priya did where we have all the ingredient and where we had food, GRAS, tox, and irritation/sensitization and just go down all the ingredients. And I think it's a very clear way of accounting for all the ingredients in what we have.

Because in these I think wheat being a food, per your question, Wilma, if we can say these are all ingested in foods, then we don't need the systemic tox presumably.

MS. BURNETT: So, with food items that have been consumed for millennia and are known to be safe, there won't be a GRAS designation, a formal CFR. There is like a blurb in the CFR saying, because this is a recognized food substance before 1950 something, there will be no GRAS desig- -- they don't put out a GRAS designation out. If it becomes an extract or something that's been chemically manipulated, that is in food, then there will be a GRAS designation usually.

In here, they've manipulated the food just to extract the gluten out, so that's why there's a CFR designation for GRAS. But, for the flour or anything like that, there won't be.

DR. BERGFELD: Maybe we need another column in this chart that's been made up on page 5 in the PDF. And just to have it as food or something like that.

DR. MARKS: Yeah, that's what actually Priya has, the first column as GRAS, the second is food, third is tox.

DR. SLAGA: That would include food additives, right.

DR. BERGFELD: Yeah.

DR. MARKS: And, again, I found that very helpful.

MS. BURNETT: And that's the data profile page?

DR. MARKS: Yes.

DR. BERGFELD: Okay.

DR. HELDRETH: In an instance like this -- first, let me talk about the one with Priya with the algae. We're often looking at the extract or the water and we're considering the food use of that genus in species regardless of the endpoint here. So, in this case with wheat, you know, we have kind of the two main parts of the wheat plant: you've got the straw or the stem, and then there's the seed.

And then all of the rest of the ingredients are some subgroup of the seed whether it be the germ or the bran or break those two down further into things like bran lipids or germ extract or flour lipids. So, except for maybe the stem, everything else kind of falls under food, but it's maybe more concentrated for some constituents and less concentrated for other constituents.

So I don't know exactly how we would -- would you want essentially all of these to fall under the food category except for maybe the stem and the straw? Or would only the actual, say, seed or the actual germ really qualify to fit under the food category?

DR. MARKS: I have the leaf mentioned here. You can include the leaf under the stem?

DR. HELDRETH: You have the wheatgrass. The young leaf is --

DR. MARKS: There's a straw.

MS. BURNETT: That's the sprout. We don't know under the definition of this whether the leaf extract is the mature leaf or if it's the sprout, which is the wheatgrass that people drink.

DR. HELDRETH: Right. It gets a little harder to define the lines where food is and isn't.

DR. MARKS: And presumably the species really doesn't have an impact on this discussion.

DR. BERGFELD: Other than impurities.

DR. HELDRETH: I mean for some of these we know they're synonymous. The vulgare and the spelta and the aestivum are currently considered to be synonyms.

DR. BERGFELD: I don't know. Do we eat the leaves? I mean, normally is it ingested in any food part that we ingest?

DR. MARKS: For this, I have a feeling we may be doing insufficient.

DR. SLAGA: I think cattle do, don't they?

DR. BERGFELD: Hmm? Cattle do. They eat the whole stem and everything.

DR. SLAGA: I mean, not human, but the animals they feed.

DR. MARKS: Yeah, sure. And there would be -- again, there's lack of toxicity in the cattle side. So that's a good point, Tom.

DR. ANSELL: I would think we would want to draw the line what we're interested in as whether it's a part of the human diet. And I don't know the answer to what part of a wheat plant that is, but I'd stay away from cattle fodder or fish food. So limit it to historical period of the classic part of the human diet.

DR. BERGFELD: So you would remove anything that relates to the stem and the leaf?

DR. MARKS: I would, Jay, have probably the opposite. I mean, a lot of our toxicologic data comes from animals when we do the studies on them. And, in this case, just like humans eat it we don't have toxic effects. If cattle we know eat it and they don't have any toxic effects, I think we can infer that it would be safe.

So I'm not sure I would eliminate veterinary food sources from the consideration. I wouldn't use it as the primary.

DR. SHANK: No.

DR. MARKS: Obviously, I'd prefer human ingestion, but if we had animal ingestion well known and no toxic effects, to me that would be adequate. But, Ron and Tom -- Tom, you're the one that suggested the animals. I kind of like that.

DR. SLAGA: All of the wheat, oats, and barley, and all that, almost all of it's used for different types of animals. I mean, nothing seems to go to waste. Put it that way.

DR. MARKS: So, I mean, we could have it -- just again, perhaps have an insufficient data announcement and clarify which ingredients are food sources. And, perhaps, Christina, with our discussion on animals perhaps include that too.

I don't know. We'll come back to that, Ron. You were the one that moved forward with safe for all of them other than sensitivity data and I --

DR. SLAGA: I agree with that.

DR. MARKS: Do we even need to clarify this or just move forward?

DR. SHANK: I don't think that you need to clarify it.

DR. MARKS: Okay. And then I have -- there was little sensitivity data; so what I have as the vulgare germ extract was okay, we concur on that, right, Ron? Which were the three you said?

DR. SHANK: The germ extract, the gluten, wait.

DR. MARKS: Hold it a second.

DR. SHANK: The ones we have data on.

DR. MARKS: Yeah, well it's interesting because there's little sensitization data, but the germ glycerides were okay at 0.5 percent, while its use is 25 percent. But the previous report came to the conclusion it was safe.

Then the gluten was safe from previous reports and the kernel, flour and germ glycerides safe from previous reports. But, without much in terms of sensitivity data, I didn't think -- but you felt there were some HRIPTs on those?

DR. SHANK: Yeah, I don't have the page, but I have we have available negative results from HRIPTs.

MS. BURNETT: PDF page 19.

DR. SHANK: Nineteen? Thank you.

DR. MARKS: Yeah, so that's what I said, there's very little. And when I look at the spreadsheet here, when you go down where the Xs are, really there's only human dermal sensitization on the vulgare germ extract and that was okay. And human on the germ glycerides which previously was felt to be safe and its now use is 25 percent, but the human sensitization data was only 0.5 percent. So I only had really, from a sensitization point of view, the vulgare germ extract. Did I miss the other ones, Ron, that you felt there was data on?

DR. SHANK: Just those three -- the germ glycerides, germ extract, and gluten. We have data now at not as high concentration.

DR. MARKS: Right.

DR. SHANK: So, if you want more use concentrations then we should ask for it.

DR. MARKS: Yeah.

DR. SLAGA: It's the first time.

DR. MARKS: Then that would be a safe for the vulgare germ extract and sensitization for everything else.

DR. SHANK: Yes.

DR. MARKS: So that would come out as an insufficient.

DR. BERGFELD: Yeah, the announcement --

DR. MARKS: Yes. How do we handle the Type 1 reactions? And then the other is the vulgare germ extract is okay. Can we assume that if it was a germ extract from the monococcum species or the aestivum species -- let me see a -- there's at least the aestivum. That's a germ extract. We could read across for those.

Say just the germ because if you notice -- now we don't have a -- the aestivum germ extract is found in a lot of products. But the concentration of use is 0.6 percent, so way below what's been tested for the vulgare germ extract. How have we dealt with species difference before? We're assuming the ingredients are relatively the same concentration?

DR. SLAGA: Well, similar, yeah.

DR. MARKS: Yeah, similar. Yeah, okay. So I think we could -- and is there another --

MS. BURNETT: As I understand it, the aestivum and vulgare are the same plant.

DR. MARKS: Oh, we're back into that.

MS. BURNETT: Yes.

DR. MARKS: Different names for the same plant.

MS. BURNETT: Yes, the scientifically accepted name is aestivum. So, in botanical, they sometimes change names. They update them. So the vulgare's the old name. Aestivum -- so like if you -- in the VCRP data only aestivum had entries; Vulgare did not.

DR. MARKS: For the vulgare germ extract I had 40 and at higher concentrations. Maybe I'm looking at the wrong table.

MS. BURNETT: There's a little footnote saying it was listed with the nomenclature, aestivum in the VCRP database. I footnoted it; so yes, it might have reported uses for the vulgare but it got filed -- the Council survey went out for both names.

DR. MARKS: So I'll put just moving forward were a germ extract, period. So how do we deal with there has been occupational Type 1 reaction, skin and respiratory toxicity? But the conclusion for the wheat flour and starch, the reason for safety was that the cosmetic exposure was not likely to be produced as symptoms that were found in the occupational exposure. And then we have the issue of the hydrolyzed wheat protein and gluten when we limited molecular weight.

DR. BERGFELD: Since they're all wheat, you probably could take care of that in the discussion.

DR. SLAGA: Yeah. That's good.

DR. MARKS: Discussion. Okay. It sounds reasonable. Christina, clarify that at all or we'll see it in the next addition on how you handled it in the discussion?

MS. BURNETT: Could I have a little more detail on what that entails for the discussion?

DR. MARKS: Well, I think, as you can read the report from previously, that we don't think occupational Type 1 reactions, since the exposure is different than with cosmetic exposure -- much less with cosmetic exposure -- we don't think it's likely to create problems either skin or respiratory.

I guess what we need to say is we don't expect hydrolyzed wheat protein and gluten in these. Or do we repeat that the molecular -- if these are present the molecular weight needs to be limited as was in the previous report?

DR. BERGFELD: I favor the latter.

DR. MARKS: Yeah. That would be one way to handle it in the discussion. Does that sound good, Ron and Tom?

DR. SLAGA: Yeah.

DR. SHANK: Yes, it does.

DR. MARKS: Okay. So tomorrow, presumably, our team will be seconding an IDA, an Insufficient Data Announcement. And what we want is sensitization for everything other than the germ extract basically. And then we'll handle in the discussion the Type 1 sensitivities. Okay. Any other comments?

DR. BERGFELD: We also have to handle the fact that why we're not asking for the other toxicology data, because it's a food.

DR. MARKS: Yeah, absolutely. Which we'll clarify in the next look at this, when we get to the tentative report, whether or not that food will be limited to human ingestion or expanded to human and animal ingestion.

DR. ANSELL: You convinced me.

DR. MARKS: No, I think it was Tom. Tom made the suggestion. Okay. Any other comments about wheat?

DR. SLAGA: No.

DR. MARKS: Okay.

Full Team Meeting – September 17, 2019

DR. BELSITO: Okay. So this is the first time we're looking at the wheat-derived ingredients here. And, we're looking across the whole plant, looking at a number of different chemical classes, but Dan and my teammates felt that that was okay.

After reviewing the materials that we have here, we thought that there were insufficiencies for manufacturing and impurities of germ extract and wheat seed extract. That glyceride and germ extract needed sensitization and irritation. And that the data for germ extract could be used as a read-across for the other materials in this report.

So, an insufficient manufacturing and impurities of the germ extract and the wheat seed extract, and sensitization and irritation on glyceride and germ extract at concentrations of use in cosmetics.

DR. BERGFELD: Was there a second, or a comment?

DR. MARKS: Yeah, we second the insufficient data announcement.

DR. BERGFELD: Any other comments regarding the needs that have been suggested?

DR. MARKS: Don, how did your team deal with the issue of type 1 sensitivity? There are some occupational reports of both skin and respiratory, there were type 1 reactions.

And then, we have the previous assessment of hydrolyzed wheat protein in gluten, where we limited the molecular weight because of type 1 sensitivity from soaps, and I believe that was Japan. So, I think at some point in the discussion we'll have to deal with the type 1 sensitivity issue.

DR. BELSITO: Yeah, we had an extensive discussion on that. And one of the things that we asked is to go in and look at the epidemiologic data of wheat allergy and the incidents of airborne wheat reactions among individuals in occupational settings with this. Because there is not a large body of data that we're aware of with these reports.

But, yes, we had an extensive discussion not only on that, but what inhalation would do in terms of individuals who are gluten-sensitive as well as individuals who have IgE-mediated reactions to wheat protein as well.

DR. MARKS: Yeah, in the previous reports there was -- at least one of the reasoning was that the cosmetic exposure is not likely to produce a type 1 reaction. But now we have this exposure to a soap in Japan, where there were -- obviously that's a personal care product exposure -- and there were type 1 --

DR. BELSITO: That was hydrolyzed.

DR. MARKS: Yes.

DR. BERGFELD: Any other comments?

DR. MARKS: Yeah, so the read-across -- just to clarify, although this will be in the minutes. You felt you could read across the germ extract for sensitivity to the leaf, to the seed, to the bran, to the flower, to the sprout? You thought that was all okay?

DR. LIEBLER: The seed ingredients. The seed encompasses the bran and the stuff inside, which includes the germ, right?

DR. MARKS: Yeah, we had that same discussion.

DR. LIEBLER: And so, not the sprout and the leaf because those are different parts of the plant.

DR. MARKS: Okay.

DR. BELSITO: So, did we have enough data? Because I didn't have down that there was an insufficiency for the -

DR. SNYDER: We needed everything on the sprout.

DR. BELSITO: Oh, that's right.

DR. LIEBLER: Yup.

DR. MARKS: Okay, that clarifies it.

DR. LIEBLER: There was some information on the leaf in the report.

MS. BURNETT: Could you repeat the needs again for me?

DR. BERGFELD: Could you repeat the needs?

DR. BELSITO: Yeah. So, insufficient for manufacturing and impurities for the germ extract and the seed extract, sensitization and irritation for glyceride and germ extract, and everything for the sprout. Everything meaning, manufacturing, impurities, sensitization and irritation.

DR. BERGFELD: Agree?

DR. MARKS: Yes.

DR. BERGFELD: I'll call the question then, if there are no other comments. All those in favor? Unanimous, thank you.

JUNE 2020 PANEL MEETING – DRAFT TENTATIVE REPORT

Belsito's Team Meeting – June 8, 2020

DR. BELSITO: Okey-doke. So now we're moving on to wheat. And at the September meeting we reviewed the safety of 27 ingredients in the report and issued an insufficient data announcement -- long one -- method of manufacturing, composition, impurities for wheat germ extract, wheat seed extract, wheat seed -- two different variants of wheat seed -- that's three different wheat seed extracts -- wheat germ extract, wheat seed, another vulgare wheat seed extract, sprout extract, irritation and sensitization data, maximum leave-on use concentration for the aestivum wheat germ extract but in the vulgare wheat germ extract and the vulgare wheat sprout extract and wheat germ glyceride. And we were told that the -- if I am remembering this correctly now -- the aestivum and the vulgare are essentially named for the same thing. Is that correct?

MS. BURNETT: Correct.

DR. BELSITO: We haven't gotten any of the requested data, other than clarification that supposedly aestivum and vulgare are essentially the same. So where are we here? We also had do the size of the hydrolysate -- to make it similar to what we did with the wheat protein and wheat gluten -- restrict peptides to an average molecular weight of 3500 Daltons or less?

DR. LIEBLER: My impression, that was an issue really pertaining to hydrolyzed wheat protein.

DR. BELSITO: Right.

DR. LIEBLER: As opposed to wheat proteins. So these aren't -- none of these are hydrolyzed, right?

DR. BELSITO: So then you don't feel that language is need, Dan?

DR. LIEBLER: No. We can -- I think the council memo suggests we can mention it in the discussion because it something that would occur to anybody who's read the other report. But I think it's fair to say that these are essentially the protein extracts that are not otherwise modified. Whereas the hydrolyzed involved introducing the risk of adverse effects from the low molecular weight hydrolysis products. Those are not in these ingredients. And we can simply state that in the discussion.

DR. BELSITO: Okay. So just point that out in the discussion that we didn't include that because we're not looking at hydrolyzed proteins.

DR. LIEBLER: Yeah. It's not an issue an issue for the (inaudible).

DR. BELSITO: Okay. And then council pointed out that in the old report we had an HRIPT on a product of 2 percent wheat germ glyceride. And the new maximum-use concentration is 0.2. So they felt we didn't need dermal irritation and sensitization data for this and that the only irritation sensitization data that was missing was for wheat sprout extract. Because we have -- for wheat germ extract in the report, we're told that -- or the vulgare wheat germ, we're told that the aestivum is the same as vulgare. And we have data from wheat germ glycerides in the old report. So basically that just leaves irritation and sensitization for the wheat sprout extract.

DR. SNYDER: I believe we still need method of manufacturing and composition for that, right? Too? For the wheat sprout extract? I have that we need the method of manufacture, composition, impurities and sensitization/irritation for wheat sprout extract.

MS. BURNETT: Yes.

DR. BELSITO: Let me see.

DR. LIEBLER: We had method of manufacture and impurities as an insufficiency for several ingredients. And as I look through the composition and impurities section, there are several references to the kinds of extracts that were tested and (inaudible) data. For example, on PDF page 33, you've got several -- a couple in a row that are shown to be -- are quoted as extracted with 80 percent methanol. Then there's additional text indicating -- below that -- a study in Triticum vulgare flour extract below -- the middle of page 33 -- mix of components that were identified depending on the solvent system used.

So I guess the question if have is whether or not any of this information could be used to help cover us with method of manufacture, where we just really have almost nothing on extracts. So method of manufacture we got the bran extract -- this is the bottom of PDF 32. We got the bran extract and then kernel flour, wheat germ and wheat gluten.

So the bran extract is kind of maddeningly imprecisely described. "Extracted at considerate temperatures." It doesn't say with what. "Resulting material is sterile filtered and then glycerin propylene glycol or soybean oil were used as solvents for these products." I assume the finished products, not as the extracted solvent.

So we just don't really have good method of manufacture information. I think the impurities, as described on this page, probably are okay to cover sort of the wheat germ seed kinds of ingredients, whether it's the flours or the extracts. (Inaudible) sprout without supporting the data.

Let's see. We do have -- I'm sorry. Actually the sprout, bottom of PDF 33, is hydroalcoholic extract, and then further acetone extraction, describe some of the components, usual suspects, I guess. So I think that's probably okay there. And so if I go back to the draft discussion, the ones -- Triticum aestivum, germ extract, seed extract, seed extract durum, seed extract vulgare germ extract, seed extract -- (Inaudible) probably hydroalcoholic extracts for all of these. I think the composition information we have is okay if we make the assumption that those hydroalcoholic extracts used to describe the composition actually represent what manufacturer typically is for these ingredients.

What's maddening here is that we just don't have any statement from any of the producers on the extraction methods. If we even had a couple, I think that would suffice to cover the whole family. So in other words, my

problem at this point is method of manufacture. And then composition/impurities is probably okay. And as a panel, we can discuss how much we want to be hung up on the method of manufacture per se, but it's something that I think we should expect for widely used ingredients like this.

DR. BELSITO: Okay. So where are you, Dan? So we need method of manufacture for all of them except the bran; is that correct?

DR. LIEBLER: Actually, I think we could have method of manufacture for even a couple representative high-use wheat germ seed and/or bran extracts. And then I would be okay as saying that those are representatives of the group because we know that almost all these kinds of ingredients are hydroalcoholic extracts or aqueous extracts. But we just don't have anything in this report that explicitly states that. Like I said, we've only got this vulgare wheat bran extract at the bottom of PDF page 33 with this very vague description.

DR. BELSITO: So you would like even the wheat -- you don't think even the bran is adequate.

DR. LIEBLER: Right.

DR. BELSITO: So then what you're asking for in terms of this insufficiency is you're getting rid of composition and impurities, but you're asking for manufacture. Is that correct?

DR. LIEBLER: That's right.

DR. BELSITO: For all of them or --

DR. LIEBLER: Well, we can ask for all of them, and then we can probably be satisfied with some significant representation of what we got. I don't want to dip our hand too much. But basically, that's what I think we need.

DR. BELSITO: Okay. So we're asking -- at this point, we're dropping composition and impurities, and we're asking just for manufacturing for everything that's there, understanding that the vulgare and the aestivum are essentially the same material.

DR. LIEBLER: Correct.

DR. BELSITO: Okay. So maybe we should make a note of that at some point in this document that it's been brought to our attention that Triticum aestivum and Triticum vulgare are essentially the same material. And therefore, those are redundant. But we're asking for method of manufacture for these. And then we're also asking for, at this point, just sensitization on the sprout. Correct?

DR. LIEBLER: That's correct.

DR. BELSITO: So method of manufacture for everything we asked for before. We can drop the composition and impurities. And we're asking for irritation and sensitization on the Triticum vulgare sprout extract. Otherwise, everything else is sufficient.

DR. SNYDER: Well, not method of manufacture for everything, Don. According to Dan, he'll be happy with a method of manufacture on the higher use ingredients that we don't have data for.

DR. BELSITO: But he said he didn't want to specify. Well, I guess we should these. We got method of manufacturer in our low-use ingredients. Would that be satisfactory to you, Dan?

DR. LIEBLER: Yes, it would.

DR. BELSITO: Okay. So we're asking for method of manufacturing on all, and we'll see what we get and decide when we see it.

DR. SNYDER: That's the best way to put it.

MS. BURNETT: This was already an IDA. So we would be looking for an insufficient conclusion now, correct?

DR. HELDRETH: Yes.

DR. BELSITO: So this would go out as a final at the next --

DR. HELDRETH: This would go out as a tentative report with an insufficient conclusion.

DR. BELSITO: Okay.

DR. LIEBLER: Are we getting feedback from industry that these are proprietary extracts, so they're uncomfortable sharing any information? Are you getting any of that, Bart?

DR. HELDRETH: We're not getting -- everything we get, we've given to you. If we don't know -- it seems likely if I were to guess that they don't want to give away all the details. But we don't know.

DR. LIEBLER: Because it's going to be deleterious from their standpoint I would imagine is you're going to have an insufficient data to reach a conclusion of safe as used based on method of manufacture. There ought to be -- I think there's a way to thread this needle without being really highly precise about how they get their magic wheat extract. If we simply had some documentation from manufacturers that this was an alcoholic aqueous extract or was an aqueous extract boiled or it is was, you know -- whatever it is, I think there's a way to present that information without giving away the store.

Because we do have sufficient information, I think, to talk about composition and impurities. But I just hate to fold on our basic information requirements we have for reports from others. You know, there's nothing special about wheat. We do this for lots of other ingredients, and we get it.

DR. BELSITO: Agreed. Anything else, Paul, Curt?

DR. SNYDER: No.

DR. BELSITO: Okay.

MS. BURNETT: I'm sorry. The draft discussion is okay and just add the language on the modified protein extracts and how that doesn't apply here?

DR. BELSITO: Yes.

MS. BURNETT: Okay.

DR. SNYDER: That looks really good.

DR. BELSITO: And I was fine with the other comments from council.

MS. BURNETT: Okay.

DR. BELSITO: You're all set, Christina?

MS. BURNETT: Yes.

Marks' Team Meeting – June 8, 2020

DR. MARKS: Some of us may have had wheat for lunch. Okay. Oh, yeah. This one's going to -- hey, Ron Shank, I'm going to rely on you to keep me straight on this one. Let me see. In September 19th, the Panel reviewed the safety of 27 ingredients with an insufficient data announcement under method of manufacture, composition, and impurities on a number of the wheat ingredients and then dermal irritation and sensitization at max leave-on concentration for another set of wheat ingredients.

None of the requested data have been received. And then it was interesting in Christina's -- Christina, you're -- I think you're the queen of these botanicals. I'll never forget you and citrus. Then you said in your memo accepted

scientific name for both Triticum Vulgare, spelta, and aestivum. You can see how bad I am with languages. I assume they're all same, and we could use read across. It's just they have different species name, but, in reality, they represent the same as the aestivum. Is that correct?

MS. BURNETT: Yes, Triticum Vulgare and spelta.

DR. MARKS: Okay. So that may help in terms of -- so let me make a couple of my comments, and then I'll throw it out. Let me see. I guess one of the things sort of was can we take the seed bran germ and flour and read across for gluten protein peptide triglycerides and then separate out leaf, sprouts, stem, and straw that we couldn't read across? Let me see.

I had safe for TV gluten, wheat germ glyceride, TV kernel flour, and they have been reported safe previously. So I just went with that, and everything else I had separate. The rest was insufficient for either method of manufacture, composition, impurities. Patient sensitivity were the missing data points.

But I really value my team members' input on this because I was getting lost in the wheat fields perhaps, as I was walking through trying to decide which was necessary. Ron, you always create a box and check things off and stuff, and my box -- I had multiple different colors in it, but we can start.

Lisa, Ron, Tom, any one of you can start. Perhaps, Lisa or Ron because we can understand. Your audio works well. Tom, I'm going to ask you to just chime in at the end.

DR. SLAGA: Okay.

DR. MARKS: So Lisa, Ron, those were my thoughts. I just reaffirmed what was found safe before because I thought we had enough data for them, and all the rest were these insufficient data that was listed in Christina's memo. But that can certainly -- I'm all ears to hear how you want to -- I must say this was probably the most pragmatic set of ingredients -- or problematic set of ingredients for me.

DR. SHANK: Okay. I think the conclusion is it's an insufficient data report, and the insufficiencies are listed nicely in the discussion. There is one problem in that the Vulgare germ, Vulgare gluten extract, and sprout extract have no concentrations of use. So when we say we need sensitization data at the maximum leave-on concentration, there is no concentration listed. So we have to change that somehow.

And you can use the maximum concentration of germ extract at 13 percent in the leave on as the benchmark. And the others -- the insufficient ones have to be tested at that concentration. But you can't just say we need sensitization at the maximum concentration of use when there is no use concentration. That's the only comment in all of that that I have.

DR. PETERSON: Yeah. I don't have much to add. I guess the only impurity that's not really addressed is pesticides. And given that, you know, there's Roundup Ready wheat, I'm just worried about pesticides, so I don't -- that was my only other comment. But I agree with the insufficiencies that were named.

DR. SLAGA: Same here with insufficiencies.

DR. EISENMANN: I just want to be sure that you know that there is an HRIPT on the product containing 13 percent Triticum Vulgare wheat germ extract in the report.

DR. PETERSON: Right.

DR. MARKS: And then, Ron, you're feeling -- yeah. Thank you, Carol -- and you're feeling was, even though there have been previous reports was safe, since we're relooking at this that that conclusion really was inaccurate for TV gluten and the wheat germ glyceride, and the TV kernel flour?

I don't have any problem saying moving forward with a tentative report with an insufficient conclusion for all these for the needs mentioned below and taking in consideration your caveat on irritation and sensitization. But is there a reason why we felt three of these ingredients were safe before and now they aren't? I guess because we really didn't

have enough data. I think I'm correct. Am I not in that they were -- those three were considered safe before in previous reports? Is that correct, Christina?

MS. BURNETT: Yes, these were some of the first reports that were published by the CIR. And yes, they were reviewed back in 1980, and they were rereviewed in 2003.

DR. MARKS: Well, I guess this is the new better.

DR. SHANK: 1980?

MS. BURNETT: Yes.

DR. SHANK: 40 years?

DR. MARKS: And 2003.

DR. EISENMANN: And in the original report, there's studies on 2 percent wheat germ -- sensitization studies, 2 percent wheat germ glycerides in over 1,000 people. And now the maximum use concentration is 0.2 percent of wheat germ glycerides versus 2 percent. So I think that would be covered, at least the sensitization parts of it.

DR. SHANK: Wheat germ glycerides isn't listed as insufficient. I don't see it. Oh, yeah, at the very end.

MS. FIUME: To that point, is the TV gluten or kernel flour listed as insufficient? Am I missing those in the list of insufficiencies?

MS. BURNETT: Which ingredients again, Monice?

DR. MARKS: Yeah. What Lisa's -- see, that's why I said safe for the TV gluten, the wheat germ glyceride, and TV kernel flour and all the rest could be as insufficient.

DR. PETERSON: Yeah. I would support that, the distinguishing between --

MS. FIUME: So then, is it correct, as it stands, the wheat germ glycerides would need to come out of the current insufficient data listed ingredients, but the Triticum Vulgare gluten and kernel flour were never listed as insufficient after the September meeting?

DR. MARKS: Yes.

MS. FIUME: Do I have that correct, Christina?

MS. BURNETT: Correct.

MS. FIUME: Yeah.

DR. MARKS: That's what I mean. So again, going back to what I said at the beginning that we move that a tentative report be issued safe for TV gluten, wheat germ glyceride, TV kernel flour, that's based on previous reports, and then all the rest of the ingredients insufficient for either method of manufacture, composition, impurities, and/or irritation and sensitization where there is missing data points. Is that a -- Ron, Lisa, keep me straight on that. Does that sound -- I basically think back off of previous reports and said if it was safe in the past -- I know, Ron, you kind of raised your eyebrow when you said 1980. When did you start on the Panel, Ron?

DR. SHANK: Ha, no, I wasn't -- even I wasn't on the Panel then.

DR. BERFELD: I was.

DR. MARKS: Huh. And then -- well, Wilma was. Yeah. And then in 2003 -- so at least this century, we had a reaffirmation of their safety. And I'm sure tomorrow, we're going to have input from the Belsito team too. But do you like that division, Ron, Lisa? And then, Tom, ultimately somewhere I want your input, but your audio is generally terrible, actually.

DR. BERGFELD: Can I ask a question?

DR. MARKS: Sure, Wilma.

DR. BERGFELD: In the other wheat products, we have been concerned with molecular weights, and we do have proteins and amino acids in some of these products that we're looking at -- ingredients that we're looking at. We've not even mentioned that. Is there a reason for that, or we have no concern about that? We have molecular weights and sensitization.

DR. SHANK: Well, I'm not concerned with --

DR. PETERSON: How can you have a molecular weight?

DR. SHANK: None of these are hydrolysates.

DR. BERGFELD: Okay.

DR. SHANK: And the issue with the wheat protein hydrolysate was the size of the peptides. And I don't think that's an issue here.

DR. BERGFELD: Okay. Would that be any reason to put that in the discussion, or is that just a no-issue?

DR. SHANK: I wouldn't add it to the discussion; it might just confuse things.

DR. BERGFELD: Okay.

MS. BURNETT: Do we have other items for the discussion besides what I have drafted?

DR. SHANK: Not from me. We still have the problem of doing sensitization -- asking for sensitization data when we don't have a use concentration.

MS. BURNETT: Okay.

DR. MARKS: Okay.

DR. SHANK: The only way I can see out of that is to use the use concentration for the germ extract, the 13 percent in leave ons. Pardon me. So we could use 13 percent for the irritation and sensitization data. Pardon me.

DR. MARKS: And that would be addressed in the discussion, Ron.

DR. SHANK: In the discussion.

DR. MARKS: Yep.

MS. FIUME: And that would be completely consistent with what we do in the conclusion when something is safe and we don't have a concentration of use. We do direct it to what we do know, so that would be very consistent.

DR. SHANK: Correct.

DR. MARKS: Yep.

DR. SHANK: Pardon me.

DR. MARKS: So Lisa, Ron, Tom, are you -- I know we've had a lot of discussions. Are you okay with three of these ingredients safe and the rest are insufficient?

DR. PETERSON: Yes.

DR. SLAGA: I am, too.

DR. MARKS: So that would mean three are safe, 24 are insufficient, and we'll see what the Belsito team feels tomorrow.

DR. EISENMANN: Can you just --

DR. MARKS: Any other comments? Tom? Does that sound good to you?

MS. BURNETT: Just a second. So because the Vulgare and the aestivum are actually synonymous, the safety could be extended to the ingredients that are similar?

DR. MARKS: Let me see. TV Vulgare gluten.

MS. BURNETT: I guess there is --

MS. FIUME: Christina, I didn't see overlap between those, did you?

MS. BURNETT: Yeah. You're right. No, I was looking at -- the flour lipid stuck out at me.

DR. MARKS: Yeah. That's what I was looking. I didn't see an overlap either.

MS. BURNETT: All right. Never mind.

DR. MARKS: Okay. No, thanks for bringing it up because, if it doesn't come up now, it will come up for the final draft. It's always better before we get to the final. Any other comments, Tom? Again, Tom, it's hard to hear you. Okay to proceed the way I mentioned?

DR. EISENMANN: I just have one question. I'm not sure I understand. Triticum Vulgare wheat germ extract, for which you have an HRIPT on a product containing 13 percent that's negative, is that still insufficient for the sensitization data?

MS. BURNETT: No. Wait, what?

DR. EISENMANN: It was in the report -- it's been in the report for a while, even though it was in the report before.

MS. FIUME: It's PDF page 37 in the middle of the page.

DR. MARKS: What about that, Carol? We still need -- you're talking about the TV germ extract?

DR. EISENMANN: Yes.

DR. MARKS: Yeah. The sensitization of that's fine.

DR. EISENMANN: Okay.

DR. MARKS: Yeah. It was 15 percent as okay, but we still have method of manufacture. We don't have composition. We don't have impurities.

DR. EISENMANN: Okay. I just --

DR. MARKS: It still remains insufficient. That's why I worded it to let Christina sort that out ultimately as to, you know, we don't need sensitization data on that ingredient because we already have it.

DR. EISENMANN: Okay. I just wanted to clarify it, because in the last version, you did ask for sensitization data on it when it was already in the report.

DR. MARKS: Okay. Thanks. Nope, we don't need it.

DR. SHANK: We asked for germ, not germ extract.

DR. MARKS: No, under dermal irritation and sensitization, look at the middle of that sentence: TV germ extract. Carol's exactly right; we did ask for that. It was the second ingredient on the second line under the needs of dermal irritation and sensitization. So any rate, we'll clarify that, Carol and Christina.

MS. FIUME: Hey, Jim, so that we have it correct in the discussion, then should the request for dermal irritation and sensitization for Triticum aestivum wheat germ extract be removed for dermal irritation and sensitization since it's assumed they're equivalent?

DR. MARKS: Yes. Thank you for pointing that out. I told you this kind of reminded me of a whack-a-mole: one of those games where something would pop up and you'd hit it and then there was another one that popped up. Okay. Tom, I keep asking you and then somebody brings up another issue. It's like that whack-a-mole man keeps popping up.

Tom, are you okay then? We're, obviously, for Christina and ourselves, clarifying what the insufficiencies are. I think we've got that straight.

I'm not going to read all our -- suggest reading all that tomorrow. Christina, if they ask that, I'm going to ask you to list those as you've heard from our team. Tom, you okay with proceeding forward with a tentative report with a conclusion: three safe, 24 not?

DR. SLAGA: Yeah.

DR. MARKS: Insufficient I should say, not not insufficient. Does that sound good?

DR. SLAGA: Yeah. I agree with that.

DR. MARKS: Okay. Good. Thanks. Any other comments? One more whack at this game. Okay. Let's move on to the next ingredient then. I'm glad it's going to be a tentative report because it gives us another crack at wheat.

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DR. MARKS: Well, Wilma, you said MI was going to be a problem; wheat's a problem for me. I get glutens hypersensitivity when I look at these Wheat ingredients. Because there are 27 of them, and I'm looking at Christina's September 2019 review where the Panel issued an insufficient data announcement. And, there were a number of ingredients that we wanted method of manufacturing, composition and impurities. That was in Christina's February 21, 2020 memo. So, again, it's from September 2019.

And then, none of the requested data was received, but in Christina's memo she indicates that Triticum Vulgare, Triticum Spelta, and Triticum Aestivum are the same. And so, obviously, now when we have to look at these ingredients we got to say, well they have a different name but they're really the same.

So, dealing with these, what our team proposes is that we issue a tentative report at this time. I and the team felt that we could move forward with three of the ingredients are safe, the Triticum Vulgare Gluten, the Wheat Germ Glycerides and the Triticum Vulgare Kernel Flower. That largely because they came from previous reports and were felt to be safe in the previous reports, and we just concur with that.

The remaining 24 ingredients, even though the names are the same and repetitious, there are still insufficiencies. And, I asked Christina, in this next rendition when we see the tentative report, that method of manufacture, composition, impurities, irritation and sensitization, where they are missing data points, those are the ingredients that should be listed under that. So, I tasked her with that. I didn't go down and tallied each one.

So the motion is to move forward with a tentative report, three safe, the rest, 24 insufficient. And, Don, I expect your team, in looking at these ingredients, had a slightly, maybe not slightly, had a different endpoint, and I'm sure will come to a similar conclusion.

DR. BERGFELD: So, that's a motion. Don, you want to respond?

DR. MARKS: But, as in the past, if the Belsito team has a different motion and we concur, I'll withdraw my motion. I'd be surprised if we concur.

DR. BELSITO: Hopefully I captured this correctly, but we came out with needing manufacturing for all of the ingredients.

DR. SNYDER: Well, Don, we said method of manufacture for a couple of the high-used ingredients. If they were similar enough, we probably thought we could clear them all.

DR. BELSITO: Right. But, we said give us all for now, then we'd clear it up.

DR. SNYDER: That's correct.

DR. BELSITO: And, then we just had a discussion about, except for the Sprout, we pretty much had sensitization and irritation for all of them. And the question, and I don't remember what we decided, whether we were going to ask for sensitization and irritation on the Sprout or just manufacturing.

DR. SNYDER: Sensitization and irritation on the Sprout.

DR. BELSITO: Right. Okay, and method of manufacturing for all.

DR. BERGFELD: So, is the motion being amended, or where --?

DR. BELSITO: Well it's slightly different because the Marks' team is clearing three of these ingredients. Is that right, Jim? And we're clearing --

DR. MARKS: Yeah, that's right. And that was largely based on, in my review that they had been declared safe before. So, I didn't go back -- Christina, in the spreadsheet that has all the toxicological endpoints, including DART, genotox, and sensitization, under Triticum Vulgare Gluten, which previously had been declared safe, you have an asterisk under method of manufacture. Look at that asterisk, "indicates data were available in previous report." So, that's why I felt method of manufacture wouldn't be needed if you look on Christina's spreadsheet.

DR. SNYDER: In the report on Page 31, at the bottom of the list of all of the ingredients, there are the three asterisks you mentioned that were previously (audio skip).

DR. MARKS: Yeah, so that's why I didn't feel we need method of manufacture if it were (audio skip). And, with the Gluten, we have sensitization at one percent, which was okay. It's used at .05 percent. And on the Wheat Germ Glycerides, again, was safe previously. And, we have sensitization data on two percent, which was okay. That's used at 0.2 percent.

To me, probably the biggest concern was the Wheat Kernel Flower, again, Christina has method of manufacture, and we have that for the Wheat Kernel Flower. We didn't have the sensitization data, but I thought perhaps we could read across on that. So, that's why I thought those three could be declared safe, and then the rest insufficient.

DR. LIEBLER: Can I make a comment on method of manufacture here? If you look at PDF Page 32, which has the method of manufacture, there are four ingredients listed and the first one is an extract and the others are flowers, or solids, basically.

And, most of our ingredients are actually extracts. And the one extract we have shown here is very imprecise in terms of what is done. Now, I realize that there is probably some secret sauce in preparing these, some proprietary information. But it would be good for us to know -- I mentioned the possibly high-used ingredients, but at least some representatives of the extracts as to whether these are hydro-alcoholic extracts, aqueous extracts. If we had some of that kind of information, we could get an idea of what is the type of approach used for this. None of it would be surprising, but right now it's just plain undocumented.

And then, we have enough information, I think, in some of the impurities and composition that we might be able to buttress our understanding of what these extracts are. So, myself, that's what I'm really looking for in the next version of this report.

DR. MARKS: Dan, did you go back and look at the original reports and see what they had in that for method of manufacture? Would that meet your needs?

DR. LIEBLER: I did not.

DR. BELSITO: It's on PDF Page 50. It says, "Wheat Flower is the milled flower grain endosperm." It's a fine, soft powder that contains carbohydrates, proteins and approximately 12 percent moisture. It gives some constituents. That's it for Wheat Flower. Then it says, "Wheat Starch is the amylose and amylosepectin-rich portion of Wheat Flour." Then it contains this, carbohydrates, 86 to 91, and 9 to 13 percent moisture."

So the manufacturing is dense that these are -- what we're looking at now are extracts, they are not these powders that were milled. And, that's it. So, we don't know what they're extracted with. So these are a little bit different than what we were looking at before.

DR. BERGFELD: So, what you're doing, Don, is supporting your request for insufficient because of manufacturing information that you needed?

DR. BELSITO: You broke up a little bit, Wilma; I didn't hear what you were saying.

DR. BERGFELD: I said, so you've been supporting your premise that the method of manufacture is needed for all of these, making it insufficient.

DR. BELSITO: We're just asking at this point for method of manufacturing for all, and sensitization and irritation of the Sprout. You know, like Dan said, we hoping at least to get the ones that are most frequently used.

DR. MARKS: Yeah, I have no problem with that, and, probably our team won't. Again, we'll be conservative. We're going to get another bite out of that, so this would be a tentative report with an insufficient conclusion at this point. Is that correct, Don?

DR. BELSITO: Yes.

DR. SHANK: When you ask for sensitization data on the Sprout Extract, at what concentration you want, because no concentration is listed in the table.

DR. BELSITO: Well, you know, hopefully we can get some idea of what the concentration is because the company that would have that data would presumably be using it around that concentration. It's a good point, though Ron. It would be the concentration of use.

DR. MARKS: Ron, why don't you mention how you handled that yesterday.

DR. SHANK: My suggestion was the Panel might use the concentration of 13 percent, which is the maximum concentration for Germ Extract in leave-ons, as a guide to industries to what they would provide for a sensitization study.

DR. LIEBLER: Fair enough.

DR. BELSITO: I'm fine with that.

DR. SHANK: Okay.

DR. BERGFELD: So, Jim, you restated your original motion; you've made a new motion.

DR. MARKS: Yes.

DR. BERGFELD: And, we've had, I think, an added suggestion of method of manufacture for all ingredients, and concentration of use.

DR. MARKS: And I seconded that motion.

DR. BERGFELD: Okay, Don made that motion; you seconded it. Any further discussion regarding Wheat going out as an insufficient data announcement?

DR. HELDRETH: Dr. Bergfeld, we can actually send this out as an insufficient data conclusion in a tentative report.

DR. BERGFELD: Okay. Thank you. Any other discussion regarding this conclusion and this action? All those in favor of this motion and the discussion points, raise your hand. Thank you. Any opposed, be verbal please. Unanimous, then, it goes out as an insufficient data conclusion.

Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics

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The Expert Panel for Cosmetic Ingredient Safety members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; David E. Cohen, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; Lisa A. Peterson, Ph.D.; Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. Previous Panel member involved in this assessment: James G. Marks, Jr., M.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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ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 27 wheat-derived ingredients. Most of these ingredients are reported to function as skin conditioning agents in cosmetic products. Industry should continue to use good manufacturing practices to limit impurities that could be present in botanical ingredients. The Panel reviewed the available data to determine the safety of these ingredients, noting the lack of method of manufacture data for all ingredients and dermal irritation and sensitization data for one ingredient, and concluded that the available data are insufficient to make a determination of safety for these wheat-derived ingredients under the intended conditions of use in cosmetic formulations.

INTRODUCTION

Most of the wheat-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, absorbents, antioxidants, bulking agents, film formers, flavoring agent, hair conditioning agents, and viscosity increasing agents, according to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*; see Table 1).[1] Functions such as skin bleaching agent (for Triticum Vulgare (Wheat) Germ Extract) are not considered cosmetic functions in the United States (US) and, therefore, are not addressed in this assessment. This assessment of the safety of the following 27 wheat-derived ingredients is based on the data contained in this report:

Triticum Aestivum (Wheat) Flour Lipids
Triticum Aestivum (Wheat) Germ Extract
Triticum Aestivum (Wheat) Leaf Extract
Triticum Aestivum (Wheat) Peptide
Triticum Aestivum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Stem Water
Triticum Spelta Seed Water
Triticum Turgidum Durum (Wheat) Seed Extract
Triticum Vulgare/Aestivum (Wheat) Grain Extract
Triticum Vulgare (Wheat) Bran
Triticum Vulgare (Wheat) Bran Extract
Triticum Vulgare (Wheat) Bran Lipids
Triticum Vulgare (Wheat) Flour Extract
Triticum Vulgare (Wheat) Flour Lipids
Triticum Vulgare (Wheat) Germ
Triticum Vulgare (Wheat) Germ Extract
Triticum Vulgare (Wheat) Germ Powder
Triticum Vulgare (Wheat) Germ Protein
Triticum Vulgare (Wheat) Gluten*
Triticum Vulgare (Wheat) Gluten Extract
Triticum Vulgare (Wheat) Kernel Flour*
Triticum Vulgare (Wheat) Protein
Triticum Vulgare (Wheat) Seed Extract
Triticum Vulgare (Wheat) Sprout Extract
Triticum Vulgare (Wheat) Straw Water
Wheat Germ Glycerides*

*Previously reviewed ingredients

The safety of Wheat Flour, now known as Triticum Vulgare (Wheat) Kernel Flour, was previously reviewed by the Panel and the conclusion of "safe … in the present practices of use and concentration" was published in 1980,[2] and reaffirmed in a re-review that was published in 2003.[3] The safety of Triticum Vulgare (Wheat) Gluten and Wheat Germ Glycerides was also previously reviewed by the Panel and the conclusion of "safe when incorporated in cosmetic products and constitute no risk to the public in its present cosmetic use of these products" was published in 1980,[4] and reaffirmed in the re-review published in 2003.[3] Because it has been more than 15 years since the safety of Triticum Vulgare (Wheat) Gluten, Triticum Vulgare (Wheat) Kernel Flour, and Wheat Germ Glycerides was reviewed, these ingredients are included in this safety assessment for re-review. Excerpts from the summaries of the 1980 reports are disseminated throughout the text of this document, as appropriate, and are identified by *italicized text.*

The Panel has reviewed the safety of several additional wheat-derived ingredients including Wheat Amino Acids,[5] Triticum Vulgare (Wheat) Starch,[2,3,6] Hydrolyzed Triticum Spelta Starch,[6] Hydrolyzed Wheat Starch,[6] Triticum Aestivum (Wheat) Germ Oil,[7] Triticum Vulgare (Wheat) Germ Oil,[3,7,8] Triticum Vulgare (Wheat) Germ Oil Unsaponifiables,[7] Hydrogenated Wheat Germ Oil,[7] and Hydrogenated Wheat Germ Oil Unsaponifiables.[7] The Panel concluded that all of these ingredients are safe in the present practices of use and concentration in cosmetics. The Panel also reviewed Hydrolyzed Wheat Protein and Hydrolyzed Wheat Gluten, and concluded that these ingredients are safe for use in cosmetics when formulated to restrict peptides to an average molecular weight of 3500 Daltons (Da) or less;[9] this conclusion is in response to reports of type 1 immediate hypersensitivity reactions that occurred in sensitized individuals following exposure to cosmetic products that contained one of these two ingredients with molecular weights greater than this limit. Polypeptides must be at least 30 amino acids long (i.e. molecular weights of about 3570 Da or more) to elicit type 1 hypersensitivity reactions (i.e. to interact with the two IgE-binding epitopes).

Most of the ingredients reviewed in this safety assessment may be consumed as food, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. The primary focus of the safety assessment of these ingredients as used in cosmetics is on the potential for effects from topical exposure. Proteins from wheat in the diet, specifically wheat gluten, are associated with adverse health conditions (such as celiac disease and dermatitis herpetiformis) in a small portion of the general population. Since the maximum dose of gluten possible from cosmetics is low, there is little likelihood that cosmetic products could precipitate a flare-up of either gastrointestinal or cutaneous symptoms.[4,10]

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

Note: In many of the published studies, it is not known how the substance being tested compares to the cosmetic ingredient. Therefore, if it is not known whether the substance being discussed is a cosmetic ingredient, the test substance will be identified as "wheat…" (e.g., wheat germ extract or wheat flour); if it is known that the substance is a cosmetic ingredient, the *Dictionary* nomenclature "Triticum Aestivum…" or "Triticum Vulgare…" (e.g., Triticum Aestivum (Wheat) Germ Extract or Triticum Vulgare (Wheat) Kernel Flour) will be used. Of additional note, the accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum*.[1,11]

CHEMISTRY

Definition and Plant Identification

The definitions of the ingredients included in this review are provided in Table 1.[1] *Triticum* wheat species have been used as food staples for 10,000 years and originated in the Middle East.[12] *Triticum aestivum* L. is the most cultivated cereal grain in the world, making up about a third of total cereal grains. [13] *Triticum monococcum* is also known as eikorn and is native to eastern Europe and western Asia.[12] *Triticum turgidum* var. durum is also known as durum wheat, hard wheat, or macaroni or pasta wheat, and is commonly cultivated in the Mediterranean region.[11,12] *Triticum spelta* is considered to be an ancient wheat grain that was once prominently grown in ancient Egypt and Italy and is now grown in northern and eastern European countries.[12,14] The accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum*.[1,11]

Table 2 lists the generic definitions of the parts of plants that are most pertinent to the ingredients in this report.[1] The wheat plant is comprised of a root and shoot system.[15] There are two types of roots: the seminal roots and the nodal roots (crown or adventitious roots). The shoot is made up of a series of repeating units or phytomers, each potentially having a node, a leaf, an elongated internode, and a bud in the axil of the leaf. The dry fruit of the wheat plant may be referred to as the seed, grain, or kernel. The embryo of the seed is also called the germ and is comprised of the scutellum, the plumule (shoot), and the radicle (primary root). The scutellum secretes some of the enzymes involved in germination and absorbs the soluble sugars that are breakdown products of the starch in the endosperm. The endosperm is surrounded by the metabolically active cell layer called the aleurone layer, the testa (seed coat), and the pericarp (fruit coat).

Triticum Vulgare (Wheat) Germ

Wheat germ is comprised of the embryonic axis and the scutellum of wheat seed and represents about 2.5% - 3.8% of total seed weight.[16] It is a by-product of the flour milling industry.

Chemical Properties

Triticum Aestivum (Wheat) Leaf Extract

The pH of wheatgrass (the young leaves of wheat) is reported to be 7.4.[17]

Triticum Vulgare (Wheat) Kernel Flour

The pH of refined wheat flours is approximately 6.0 - 6.1, while the pH of whole wheat flour is approximately 6.2.[13]

Method of Manufacture

Triticum Monococcum (Wheat) Stem Water, Triticum Spelta Seed Water, and Triticum Vulgare (Wheat) Straw Water

In some cases, the definition of the ingredients, as given in the *Dictionary*, provides insight as to the method of manufacture. In general, botanical waters are prepared from the leaves, stems, flowers, bark, roots, or other parts of a plant or the whole plant.[1] The condensate from steam distillation produces two distinct fractions that contain the volatile ingredients from the plant. The water insoluble fraction contains the "oil." The water-soluble fraction contains ingredients from the plant that are water soluble, and is identified by the term "Water" in the INCI name.

Triticum Vulgare (Wheat) Bran Extract

A supplier reported that its 4 different Triticum Vulgare (Wheat) Bran Extract products are derived from food-grade plant material and are extracted at "considerate" temperatures during a fixed time.[18] The resulting material is sterile filtered at the end of fabrication. Glycerin, propylene glycol, and soybean oil were used as the solvents for these products. (Table 3)

Triticum Vulgare (Wheat) Germ

Wheat germ is a by-product of flour milling and is produced by mechanical separation of the germ from whole wheat.[16]

Triticum Vulgare (Wheat) Germ Extract

A supplier reported that Triticum Vulgare (Wheat) Germ Extract is produced by solubilizing wheat germ in water.[19] The insoluble material is then removed and the extract is filtered.

Triticum Vulgare (Wheat) Gluten

Triticum Vulgare (Wheat) Gluten is prepared by water washing wheat flour then drying the insoluble matter with careful temperature control.[4] The cream-tan powder derived from this process is food grade.

Triticum Vulgare (Wheat) Kernel Flour

Wheat flour is produced by different forms of milling or grinding, of the grain's endosperm.[13,20] The different forms of compression and shear allow for producing different grain sizes for different end uses or flour types.

Wheat Germ Glycerides

Wheat Germ Glycerides are produced through the transesterification of wheat germ oil (from conventional milling processes) with glycerin.[4]

Composition/Impurities

Yields of constituents in wheat have been found to be dependent on extraction methods and growing conditions such as soil composition, climate, duration of growth period, and height at harvest.[17] Additionally, different plant parts have different constituent compositions.

Triticum Aestivum (Wheat) Leaf Extract

At least 41 flavonoid derivatives have been identified in wheat leaf extract (extracted with 80% methanol) using liquid chromatography/mass spectrometry (LC/MS).[21] The identity of flavones, a subgroup of flavonoids, comprised therein were luteolin, tricetin, apigenin, chrysoeriol, and tricin.

Triticum Vulgare/Aestivum (Wheat) Grain Extract

Total phenolic content of wheat grain extract (as 80% methanol extracts) was 5.1 - 6.8 µg (±)-catechin/mg for endosperm and embryo and 16.0 - 16.7 µg (±)-catechin/mg for "pericarb" (pericarp) and testa.[22] *Triticum aestivum* grain may be contaminated with mycotoxins such as trichothecenes and zearaleonones from toxin-producing fungi and molds.[14]

Triticum Vulgare (Wheat) Bran Extract

Descriptions of the compositions of 4 different Triticum Vulgare (Wheat) Bran Extract products are summarized in Table 3.[18]

Triticum Vulgare (Wheat) Flour Extract

The yield of non-starch lipids, neutral lipids, glycolipids, and phospholipids of wheat flour extract was dependent on the solvent system used.[23] In a study that utilized chloroform-methanol, chloroform-methanol-hydrochloric acid, chloroform-methanol-sodium chloride, methanol, chloroform, water-saturated n-butanol, methanol-chlorofrom-hexane, hexane-isopropanol, and hexane, total lipids ranged from 6.30 - 9.76 g fatty acid/kg flour, neutral lipids ranged from 3.76 - 5.43 g fatty acid/kg flour, glycolipids ranged from 1.09 - 2.98 g fatty acid/kg flour, and phospholipids ranged from 0.78 - 1.85 g fatty acid/kg flour. The five major fatty acids present in the lipid classes extracted from wheat flour were palmitic acid, stearic acid, oleic acid, linoleic acid, and linolenic acid.

Triticum Vulgare (Wheat) Germ

Wheat germ contains about 10% - 15% lipids, 26% - 35% protein, 17% sugar, 1.5% - 4.5% fiber, and about 4% minerals.[16] Bioactive constituents include tocopherols (300 - 740 mg/kg dry matter), phytosterols (24 - 50 mg/kg), policosanols (10 mg/kg), carotenoids (4 - 38 mg/kg), thiamin (15 - 23 mg/kg), and riboflavin (6 - 10 mg/kg).

Triticum Vulgare (Wheat) Germ Extract

Analyses of an aqueous mixture containing 3.5% - 12% Triticum Vulgare (Wheat) Germ Extract determined that the heavy metals content was below the acceptability threshold of 0.5 ppm, with cobalt, mercury, and lead not quantifiable.[24] No pesticides were detected in this test material.

Triticum Vulgare (Wheat) Gluten

A supplier reported that a tradename mixture containing 4.7% - 6.4% Triticum Vulgare (Wheat) Gluten also contained 7.0% - 8.0% sodium laureth sulfate, < 1.0% phenoxyethanol, < 1.0% ethylparaben, < 1.0% methylparaben, and water.[25] Microbial counts were < 100 cfu/g and mold and yeast content was < 10 cfu/g.

Triticum Vulgare (Wheat) Kernel Flour

There are four classes of protein in wheat flour: globulins, albumins, gliadins, and glutenins.[20] Gliadins and glutenins are components of gluten. Refined wheat flours may contain approximately 13 g/100 g dry weight protein, 0.8 - 0.9 g/100 g dry weight lipids, 85 g/100 g dry weight carbohydrates, and 9.5 g/100 g dry weight gluten.[13] Whole wheat flour contains approximately 15 g/100 g dry weight protein, 1.5 g/100 g dry weight lipids, 82 g/100 g dry weight carbohydrates, and 7 g/100 g dry weight gluten. Wheat flour may be contaminated with foodborne bacteria and fungi, including *Salmonella* spp., *Escherichia coli*, and *Bacillus cereus*. Wheat flour may also be contaminated with mycotoxins such as aflatoxins and ochratoxin A.

Triticum Vulgare (Wheat) Protein

Wheat proteins are classified into gluten and non-gluten proteins.[26] The gluten proteins are comprised of gliadins and high and low molecular weight glutenins. The non-gluten proteins are comprised of albumins and globulins.

Triticum Vulgare (Wheat) Sprout Extract

A hydroalcoholic extract of wheat sprouts was determined to be composed of hydrophilic compounds, such as peptides, and hydrophobic compounds, such as polyphenols.[27] Further extraction with 90% acetone resulted in the precipitation of 70% glutathione. Phospholipid classes identified from hydroalcoholic extract of wheat sprouts included phosphatidylethanolamine, phosphatidylcholine, phosphatidic acid, phosphatidylinositol, and lysophosphatidylcholine.[28] These phospholipids were characterized by a high content of essential fatty acids (α-linoleic acid and α-linolenic acid).

Wheatgrass is reported to contain chlorophyll, flavonoids, several varieties of vitamins including vitamins C and E, choline, minerals, enzymes, indoles, and a number of amino acids.[17]

Wheat Germ Glycerides

Wheat Germ Glycerides contain 30% to 40% monoglycerides with di-and triglycerides of mixed fatty acids.[4]

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, Triticum Aestivum (Wheat) Germ Extract has the most reported uses in cosmetic products with a total of 293 formulations; the majority of the uses are in leave-on skin care products (Table 4).[29] Triticum Aestivum (Wheat) Seed Extract has the second greatest reported number of uses in this safety assessment with 166 formulations; the majority of the uses are also in leave-on skin care products. All other in-use ingredients are reported to be used in significantly fewer formulations. The results of the concentration of use surveys conducted by the Council in 2017 and in 2019 indicate that Triticum Vulgare (Wheat) Germ Extract has the highest concentration of use in a leave-on formulation; it is used at up to 13% in face powders.[30,31] The maximum concentrations of use for the remaining ingredients are much lower, with the next highest concentration of use reported for products resulting in leave-on dermal exposure is 0.6% in Triticum Aestivum (Wheat) Germ Extract in “other” skin care preparations.

For the three ingredients that were previously reviewed and re-reviewed by the Panel, uses for Wheat Germ Glycerides have decreased considerably according to 2020 VCRP data, with 41 reported uses (37 of which are in leave-on products), down from 128 uses (mostly in lipsticks) reported in 2001 (Table 5).[3,29] The number of uses for the other two ingredients have only increased slightly. The maximum concentration of use range for Wheat Germ Glycerides in 2001 was 0.001% to 25%, with 25% reported in lipsticks; in 2019, the maximum concentration of use range for this ingredient was 0.041% to 0.2%, with 0.2% reported in leave-on face and neck products.[3,31] The ingredients not in use according to the VCRP and industry survey are listed in Table 6.

Wheat-derived ingredients may be used in products that can be incidentally ingested or come into contact with the eyes or mucous membranes; for example, Triticum Vulgare (Wheat) Germ Extract is reported to be used in lipstick at up to 0.13%, Triticum Vulgare (Wheat) Protein is reported to be used in eye lotion at up to 0.16%, and Triticum Vulgare (Wheat) Bran is reported to be used in “other” personal cleanliness products at up to 0.61%.[30]

Additionally, some of the ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Triticum Vulgare (Wheat) Germ Extract is reported to be used at up to 0.32% in hair spray and up to 0.11% in spray deodorant.[30] 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.[32,33] 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.[34,35] There is some evidence indicating that deodorant spray products can release substantially larger fractions of particulates having aerodynamic equivalent diameters in the range considered to be respirable.[34] However, the information is not sufficient to determine whether significantly greater lung exposures result from the use of deodorant sprays, compared to other cosmetic sprays. Triticum Vulgare (Wheat) Germ Extract is reportedly used in face powders at concentrations up to 13% and could possibly be inhaled.[30] 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.[36-38]

The wheat-derived ingredients described in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[39]

Non-Cosmetic

The FDA requires allergen labeling when major allergens, such as wheat, are included in food.[40] A major food allergen is an ingredient from a food or food group, such as wheat, that contains protein derived from the food.

Triticum vulgare is reported to be used extensively in traditional medicine to treat decubitus ulcers, burns, scarring delays, dystrophic diseases, and to accelerate tissue repair.[41] It has been investigated for anti-inflammatory properties.

Bran (source not specified) is an over-the-counter (OTC) laxative drug product.[42] Wheat germ is an active ingredient in weight control drug products; however, based on evidence currently available, there are inadequate data to establish general recognition of the safety and effectiveness of this ingredient for this specified use (21CFR§310.545). Wheat gluten is generally recognized as safe (GRAS) in the US for food (21CFR§184.1322).

Wheat leaf extract has been studied for therapeutic benefits for chronic fatigue syndrome, and for its immunological, anti-oxidative, and anti-cancer activities.[17,43] Wheat sprout extract has been studied for its antioxidant content and potential use as a food ingredient and in cancer treatments.[27,28,44] Wheat germ is used as a food supplement and an ingredient in several food products,[16] and wheat germ extract has also been studied for use in cancer prevention and treatment.[45]

TOXICOKINETIC STUDIES

No relevant toxicokinetics studies on wheat-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 wheat-derived ingredients that are reviewed 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 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. Thus, the potential for systemic effects, other than sensitization, is not discussed in detail in this report.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

Oral

Triticum Vulgare (Wheat) Sprout Extract

The effects of the water extract of wheat sprouts on spermatozoa was investigated using male BALB/c mice.[46] The mice were treated with benzo[a]pyrene (B[a]P) in corn oil (100 mg/kg bw) for 5 consecutive days via intraperitoneal injections. A control group of 19 mice only received corn oil (0.5 ml) and two groups of 3 mice only received wheat sprout extract (40 and 70 ml). Nineteen animals received the wheat sprout extract in parallel with the B[a]P treatment (3 mice received 40 ml extract, 10 mice received 70 ml extract, and 6 mice received 140 ml extract, in 18 equal doses by gavage) starting 3 d before the B[a]P treatment. Twenty-eight mice received just B[a]P. The sperm of the treated mice were examined 5 wk after the B[a]P treatment. The mice treated only with B[a]P had an incidence of 61.1% for abnormally-shaped sperm heads. The corn oil control group only had sperm abnormalities observed in 1.93%. The wheat sprout extract alone did not enhance the level of sperm abnormalities in comparison with the corn oil controls. The simultaneous treatment of B[a]P and wheat sprout extract resulted in a decrease in the percentage of abnormally-shaped sperm heads when compared to the group that received just B[a]P, but not in a dose-dependent manner.

GENOTOXICITY STUDIES

In Vitro

Triticum Vulgare (Wheat) Bran Extract

The genotoxicity potential of a wheat bran extract that was highly-enriched in arabinoxylan-oligosaccharides was assessed in an Ames test using *S. typhimurium* strains TA 98, TA 100, TA 1535, and TA 1537 and *E. coli* strain WP2uvrA, with and without metabolic activation.[47] The extract was dissolved at 100 mg/ml in distilled water and was tested at 5, 15.8, 50, 158, 500, 1581, and 5000 µg/plate. Strain-specific positive and negative control chemicals were used and yielded expected results. Wheat bran extract was not mutagenic at up to 5000 µg/plate.

The same researchers assessed the clastogenic potential of the same wheat bran extract in a chromosome aberration assay using Chinese hamster lung fibroblast V79 cells.[47] The cells were treated for 3 h or 20 h with the extract at up to 5000 µg/ml, with and without metabolic activation. No biologically significant increases in the number of cells showing structural chromosome aberrations were observed. The wheat bran extract was not clastogenic in this assay.

Wheat Germ Glycerides

The genotoxicity potential of Wheat Germ Glycerides in ethanol was assessed in an Ames test using *S. typhimurium* strains TA 98, TA 100, TA 102, TA 1535, and TA 1537, with and without metabolic activation.[48] Strain-specific positive and negative control chemicals were used and yielded expected results. Wheat Germ Glycerides was not mutagenic when tested at up to 5000 µg/plate.

ANTI-MUTAGENICITY STUDIES

In Vitro

Triticum Vulgare (Wheat) Sprout Extract

The ability of the S-30 fraction (decanted, incubated supernatant fluid) of the water extract of wheat sprouts to inhibit mutagenicity was assessed in an Ames test using *S. typhimurium* strain TA 98, with metabolic activation and in the presence of 7,12-dimethyl benz[a]anthracene (DMBA; 50 µg/plate).[46] The S-30 fraction was prepared from thawed plants by squeezing out the juice and centrifuging it for 30 min at 30,000 *g* before removing proteins with heat, concentrating by vacuum, and sterilizing. A decrease in the number of revertants was observed. No further details were provided.

In Vivo

Triticum Vulgare (Wheat) Sprout Extract

The same research group from the above study investigated the effects of the S-30 fraction of the wheat sprout extract on the ability of BALB/c mouse skin enzymes to activate DMBA to mutagenic metabolites.[46] The S-9 fraction (added to in vitro systems to simulate metabolic capability) from the mouse skin that received the wheat extract subcutaneously for 4 d (0.1 ml/d) still activated DMBA (single painting; 100 µg/mouse) to mutagenic metabolites for the *S. typhimurium* strain TA 98, but the ability was 20% lower than that of the S-9 fraction from mice that did not receive the wheat sprout extract. No further details were provided.

CARCINOGENICITY STUDIES

Co-Carcinogenicity

Triticum Vulgare (Wheat) Bran

In a 31-wk dietary study, a group of 12 male Sprague-Dawley rats received 20% wheat bran as a dietary supplement during and after administration of 1,2-dimethylhydrazine (a carcinogen) via 13 weekly subcutaneous injections.[49] Another group of 12 rats was fed the wheat bran in conjunction with administration of the carcinogen, and then switched to the control diet after 13 wk. A third group of 11 rats received a fiber-free (control) diet during the administration of the carcinogen, and then switched to the wheat bran diet after 13 wk. The control group (12 rats) received a fiber-free diet throughout the 31 wk. In both groups that received wheat bran in conjunction with administration of the carcinogen, small intestinal or colonic tumor yield was significantly greater, with benign and malignant tumors incidences increased by 3.4-fold ($p < 0.005$), adenoma incidences increased by 3.5-fold ($p < 0.025$), and adenocarcinomas incidences increased by 3.25-fold ($p < 0.05$) when compared to rats that received a control diet. Rats that received wheat bran only after carcinogen exposure had a reduced number of benign adenomas (71.4%; $p < 0.025$) when compared to the rats that received control diet. The rats fed the wheat bran during carcinogen administration and then switched to the control diet had the highest tumor yield, with 4.5 times as many benign and malignant tumors as the control rats ($p < 0.05$), and at least 6 times as many adenomas as any of the other dietary groups ($p < 0.05$).

Tumor/Anti-Tumor Promotion

Triticum Aestivum (Wheat) Leaf Extract

The effects of wheatgrass leaf extract on skin papillomagenesis induced by DMBA and croton oil were investigated in male Swiss albino mice.[50] The mice were divided into five groups of 10: Group 1 was the control group that received a single dose of DMBA (100 µl/50 µl acetone) on shaved dorsal skin followed 2 wk later by croton oil (1% in 100 µl acetone) 3 times a week for a total of 16 wk; Group 2 (pre-group) received wheatgrass leaf extract orally (20 ml/kg bw) for 7 d prior to the application of DMBA and croton oil in the manner that Group 1 received these; Group 3 (peri-group) was treated with DMBA and then received wheatgrass leaf extract for 15 d prior to receiving the croton oil, as in Group 1; Group 4 (post-group) was treated with DMBA as in Group 1 and received wheatgrass leaf extract at the same time the croton oil treatment started; and Group 5 received the wheatgrass leaf extract 7 d prior to and after the treatment with DMBA and through the treatment of croton oil until experiment end (total number of exposure days not stated). Tumor incidence, yield, and burden in Groups 2 - 5 were significantly decreased as compared to Group 1. The average latent period was increased in Groups 2 - 5, with the longest latent period being observed in Group 5.

Triticum Vulgare (Wheat) Sprout Extract

The tumorigenic effects of wheat sprout extract (S-30 fraction) were investigated using 8-wk-old male BALB/c mice.[46] Skin papillomas were initiated by painting the skin of mice with an acetone solution of DMBA (100 µg/mouse). Twice weekly treatments of croton oil dissolved in acetone (10 µl) was used for papilloma growth promotion. The mice received the promoter for 22 wk. One group of mice (n = 38) received 10 successive subcutaneous injections of wheat sprout extract (0.1 ml) starting on day 3 before DMBA treatment) with the croton oil promoter, while another group (n = 8) received the extract during the promotion period without the croton oil promoter. Further groupings involved giving mice the wheat sprout extract (0.1 ml) subcutaneously twice a week for 22 wk without the croton oil promoter during both the initiator and promoter phases (n = 13). Wheat sprout extract, when injected subcutaneously for 10 d during carcinogenesis initiation in mice, shortened the latency period from 9 to 4 wk and increased the number of skin papillomas by 4-fold. When the extract was applied to mice treated with DMBA, but did not have croton oil promotion, only one mouse developed papillomas during the 24 wk. Controls where the extract was injected alone without initiation or promotion did not produce skin papillomas (n = 17). The authors concluded that wheat sprout extract did not have initiating or promoting properties.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Irritation

Animal

Triticum Vulgare (Wheat) Germ Extract

In a cutaneous tolerance study of an aqueous solution containing 12% Triticum Vulgare (Wheat) Germ Extract, three rabbits received the test material as a single dose (0.5 ml) on the skin in accordance with Organization for Economic Co-operation and Development (OECD) test guideline (TG) 404.[24] A slight to clear erythema that was reversible within 72 h was observed in all animals. It was concluded that the test material was not an irritant to the skin. No additional details were provided.

Wheat Germ Glycerides

Mild irritation was observed on abraded rabbit skin following dermal application of different lots of Wheat Germ Glycerides.[4] Minimal skin irritation was observed in rabbits that received dermal applications of Wheat Germ Glycerides in several different cosmetic formulations. Concentrations were not provided for any of these studies.

Human

Triticum Vulgare (Wheat) Gluten

A mixture containing approximately 5% Triticum Vulgare (Wheat) Gluten and 7-8% sodium laureth sulfate was tested for irritation potential in a single insult patch test using 20 subjects.[51] The test material (160 µl) was applied as supplied to the upper back once under a semi-occlusive TruMed® patch for 48 h. A control site using water was also prepared. The skin was examined 1 d before patching, on day 3 (15 - 30 min after patch removal), and on day 4 (24 h after patch removal). On day 3 and day 4, very slight erythema was observed in 4 (20%) of the test subjects. Based on the mean daily irritation score of0.20, the study authors concluded the test material did not induce irritation and had good skin compatibility. The control site yielded expected results.

Sensitization

Animal

Wheat Germ Glycerides

Wheat Germ Glycerides (0.1% solution in olive oil) was evaluated for sensitization in a guinea pig sensitization study.[4] The treatment group comprised 6 guinea pigs that received an initial 0.05 ml intracutaneous injection and 9 subsequent 0.1 ml injections during the induction phase followed by a 2-wk rest period. The animals then received a 0.05 ml challenge injection. The test material was not a skin sensitizer.

Human

Triticum Vulgare (Wheat) Germ Extract

A human repeated insult patch test (HRIPT) of a face and body powder containing 13% Triticum Vulgare (Wheat) Germ Extract was conducted in 105 subjects.[52] The test material (200 mg) was applied to the test sites as supplied. The patches were partially occlusive and 2 cm^2 in area. Nine sequential 24-h induction applications and 2 concurrent 24-h challenge applications were made, with the challenge patches on the initial induction site and a naïve site. Challenge sites were read at 24 and 48 h post-application. No irritation or sensitization was observed.

Triticum Vulgare (Wheat) Gluten and Wheat Germ Glycerides

Mascara-base products containing up to 1% Triticum Vulgare (Wheat) Gluten were not dermal irritants or sensitizers in HRIPTs of up to 202 subjects or in in-use studies (number of subjects not reported).[4] A lipstick base containing up 2% Wheat Germ Glycerides produced reactions in 8 out of 1154 subjects: reactions were considered to be irritation. Wheat Germ Glycerides were not dermal irritants or sensitizers in HRIPTs of lipstick products and blushers at concentrations up to 0.5%. No adverse reactions were reported in in-use studies of a lipstick base containing 2% Wheat Germ Glycerides in 149 subjects.

OCULAR IRRITATION STUDIES

Animal

Triticum Vulgare (Wheat) Gluten and Wheat Germ Glycerides

Mild circumcorneal injection and mild discharge were noted after testing a mascara base containing 1% Triticum Vulgare (Wheat) Gluten in rabbit eyes: these changes were thought to be the results of foreign objects in the eye and drying of the formulation.[4] Complete recovery occurred within 72 h. Minimal to no ocular irritation was observed in rabbit studies with undiluted Wheat Germ Glycerides and in formulations containing up to 2% Wheat Germ Glyceride.

Triticum Vulgare (Wheat) Germ Extract

In an ocular tolerance study of an aqueous solution containing 12% Triticum Vulgare (Wheat) Germ Extract, three rabbits received the test material as a single dose (0.1 ml) instilled into the eye in accordance with OECD TG 405.[24] Mild irritation was observed that was reversible within 72 h. It was concluded that the test material was not an irritant to the rabbit eye. No additional details were provided.

OCCUPATIONAL EXPOSURES

Work-related sensitization (IgE-mediated) to wheat flour and grain dusts has been reported in bakery workers.[53-57] 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 flour and/or enzyme (e.g. α-amylase of fungal origin) occurs frequently.[56,57] Aside from wheat, 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.[53-57]

EPIDEMIOLOGY OF IMMUNE-MEDIATED GLUTEN AND WHEAT REACTIONS

Celiac disease affects approximately 1% of the population worldwide, including the US, with variations between countries.[58-60] Wheat allergy affects between 0.5% to 9 % of the population globally, with about 0.4% of adults in the US diagnosed with the allergy.[59,61,62] Children have a higher prevalence to food allergy to wheat compared to adults, and in Korean children, evidence of cross-reactivity or co-sensitization with barley has been found.[63-65] Respiratory IgE mediated allergies to wheat (i.e. baker's asthma or rhinitis) are often associated as occupational disease with the incidence in bakers ranging at 5% - 10% for asthma and 15% - 20% for rhinitis.[63] Bronchial reactivity to inhaled wheat proteins in adults with food allergy is very rare but has been documented.[66]

SUMMARY

Most of the 27 wheat-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, absorbents, antioxidants, bulking agents, film formers, flavoring agent, hair conditioning agents and viscosity increasing agents. Functions such as skin bleaching agent (for Triticum Vulgare (Wheat) Germ Extract) are not considered cosmetic functions in the US and, therefore, are not addressed in this assessment.

Yields of constituents in wheat have been found to be dependent on extraction methods and growing conditions such as soil composition, climate, duration of growth period, and height at harvest. Additionally, different plant parts have different constituent compositions. Wheat grain may be contaminated by mycotoxins, such as aflatoxins, trichothecenes, and zearalenones. Wheat flour may be contaminated with mycotoxins and foodborne bacteria and fungi, such as *Salmonella* spp., *E. coli*, and *B. cereus*.

According to 2020 VCRP survey data, Triticum Aestivum (Wheat) Germ Extract has the most reported uses in cosmetic products with a total of 293 formulations; the majority of the uses are in leave-on skin care products. Triticum Aestivum (Wheat) Seed Extract has the second greatest reported number of uses in this safety assessment with 166 formulations; the majority of the uses are also in leave-on skin care products. All other in-use ingredients are reported to be used in significantly fewer formulations. The results of the concentration of use survey conducted by the Council indicate that Triticum Vulgare (Wheat) Germ Extract has the highest maximum concentration of use in a leave-on formulation; it is used at up to 13% in face powders. The concentrations of use for the remaining ingredients are much lower; the next highest maximum concentration of use reported for products resulting in leave-on dermal exposure is 0.6% in Triticum Aestivum (Wheat) Germ Extract in "other" skin care preparations.

Wheat is considered a major food allergen and is required by the FDA to be labeled as such when included in food. *Triticum vulgare* is reported to be used extensively in traditional medicine and it has been investigated for anti-inflammatory properties. Bran (source not specified) is an OTC laxative drug product. Wheat leaf extract and wheat germ extract have been studied for various therapeutic effects and for use in food supplements.

Most of the wheat-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.

Wheat sprout extract (40 and 70 ml) alone did not enhance the level of sperm abnormalities in mice in comparison with controls. Simultaneous treatment of B[a]P and wheat sprout extract resulted in a decrease in the percentage of abnormally-shaped sperm heads when compared to the group that received just B[a]P, but not in a dose-dependent manner.

Wheat bran extract was not mutagenic in an Ames test at up to 5000 µg/plate, nor was it clastogenic in Chinese hamster lung fibroblasts in a chromosome aberration assay at up to 5000 µg/ml. In anti-mutagenicity studies, a decrease in the number of revertants was observed following exposure to the S-30 fraction of a water extract of wheat sprouts in an Ames test with metabolic activation and DMBA. A decrease in mutagenic metabolites was observed in BALB/c mouse skin following subcutaneous exposure to the same wheat sprout extract (0.1 ml/d) and DMBA.

Tumor incidences were increased in a 31-wk study of rats that received a dietary supplement containing 20% wheat bran during administration of a carcinogen for 13 wk when compared to rats that received a control diet. Rats that received the wheat bran after carcinogen exposure had a reduced number for benign adenomas when compared to controls. Wheat sprout extract (0.1 ml) was not an initiator or a promoter in mice that received the extract subcutaneously, were induced with DMBA, and/or promoted with croton oil in a 24-wk study. Anti-tumorigenic effects have been reported in an oral study with wheatgrass extract (20 ml/kg bw) in mice that were induced with DMBA and promoted with croton oil.

No irritation or sensitization was observed during an HRIPT of a face and body powder containing 13% Triticum Vulgare (Wheat) Germ Extract that was conducted in 105 subjects. No dermal or ocular irritation to 12% Triticum Vulgare (Wheat) Germ Extract was observed in rabbits in a cutaneous tolerance study and an ocular tolerance study, respectively.

Work-related sensitization has been reported in bakery workers. Symptoms include rhinitis, asthma, contact urticaria, and hand eczema. Celiac disease and wheat allergy affect populations worldwide. Children have a higher prevalence to food allergy to wheat compared to adults, and in Korean children, evidence of cross-reactivity or co-sensitization with barley has been found. Respiratory IgE mediated allergies to wheat (i.e. baker's asthma or rhinitis) are often associated as occupational disease. Bronchial reactivity to inhaled wheat proteins in adults with food allergy is very rare but has been documented.

No relevant toxicokinetic studies were found in the published literature; however, in general, toxicokinetics data are not expected to be found on botanical ingredients because each botanical ingredient is a complex mixture of constituents.

DISCUSSION

The Panel reviewed the botanical ingredients derived from the wheat plants *Triticum aestivum, Triticum monococcum, Triticum spelta, Triticum turgidum durum, and Triticum vulgare.* The accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum.* The Panel expressed concern about pesticide residues, heavy metals, and other plant species that may be present in botanical ingredients, and stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities.

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

The Panel noted that it had previously concluded that Hydrolyzed Wheat Protein and Hydrolyzed Wheat Gluten were safe for use in cosmetics when formulated to restrict peptides to an average molecular weight of 3500 Da or less. This conclusion was in response to reports of type 1 (IgE-mediated) immediate hypersensitivity reactions that occurred in sensitized individuals following exposure to cosmetic products that contained one of these two ingredients with molecular weights greater than this limit. However, based on the available information, none of the wheat-derived ingredients in this report are hydrolyzed and most are not even proteins. Coupled with lack of reports to the contrary or experience with such reactions to these ingredients in the clinical setting, concern over such reactions to these ingredients was mitigated. If the protein ingredients in this report are hydrolyzed in processing, then the Panel needs to be made aware of these methods of manufacturing to further assess the safety of these ingredients.

Some wheat-derived ingredients were reported to be used in spray and powder products that could possibly be inhaled. For example, Triticum Vulgare (Wheat) Germ Extract is reported to be used at up to 0.32% in hair spray, at up to 0.11% in spray deodorant, and at up to 13% in face powders. The Panel noted that in aerosol products, 95% – 99% of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or bronchial regions of the respiratory tract present no toxicological concerns for these ingredients. Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

At its June 2020 meeting, the Panel determined that data are insufficient to determine safety. The additional data needed to determine the safety of the wheat-derived ingredients as used in cosmetics are:

- Method of manufacturing data
- Dermal irritation and sensitization data at a test concentration of 13% for Triticum Vulgare (Wheat) Sprout Extract

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the available data are insufficient to make a determination of safety for the following 27 ingredients under the intended conditions of use in cosmetic formulations:

Triticum Aestivum (Wheat) Flour Lipids
Triticum Aestivum (Wheat) Germ Extract
Triticum Aestivum (Wheat) Leaf Extract*
Triticum Aestivum (Wheat) Peptide*
Triticum Aestivum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Seed Extract
Triticum Monococcum (Wheat) Stem Water*
Triticum Spelta Seed Water*
Triticum Turgidum Durum (Wheat) Seed Extract*
Triticum Vulgare/Aestivum (Wheat) Grain Extract*
Triticum Vulgare (Wheat) Bran
Triticum Vulgare (Wheat) Bran Extract
Triticum Vulgare (Wheat) Bran Lipids
Triticum Vulgare (Wheat) Flour Extract
Triticum Vulgare (Wheat) Flour Lipids
Triticum Vulgare (Wheat) Germ
Triticum Vulgare (Wheat) Germ Extract
Triticum Vulgare (Wheat) Germ Powder*
Triticum Vulgare (Wheat) Germ Protein
Triticum Vulgare (Wheat) Gluten
Triticum Vulgare (Wheat) Gluten Extract
Triticum Vulgare (Wheat) Kernel Flour
Triticum Vulgare (Wheat) Protein
Triticum Vulgare (Wheat) Seed Extract
Triticum Vulgare (Wheat) Sprout Extract
Triticum Vulgare (Wheat) Straw Water*
Wheat Germ Glycerides

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

TABLES

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

Ingredient/CAS No.	Definition	Function
Triticum Aestivum (Wheat) Flour Lipids	Triticum Aestivum (Wheat) Flour Lipids is a mixture of lipids derived from the flour of *Triticum aestivum*.	Skin-conditioning agent – misc.
Triticum Aestivum (Wheat) Germ Extract	Triticum Aestivum (Wheat) Germ Extract is the extract of the germs of *Triticum aestivum*.	Antioxidant; skin-conditioning agent – misc.
Triticum Aestivum (Wheat) Leaf Extract	Triticum Aestivum (Wheat) Leaf Extract is the extract of the leaves of the wheat, *Triticum aestivum*.	Antioxidant
Triticum Aestivum (Wheat) Peptide	Triticum Aestivum (Wheat) Peptide is the di-/tri-peptide fraction isolated from the protein of *Triticum aestivum* by ultra-membrane filtration.	Film former; hair conditioning agent; skin-conditioning agent – misc.
Triticum Aestivum (Wheat) Seed Extract	Triticum Aestivum (Wheat) Seed Extract is the extract of the seeds of the wheat, *Triticum aestivum*.	Hair conditioning agent; skin-conditioning agent – misc.
Triticum Monococcum (Wheat) Seed Extract	Triticum Monococcum (Wheat) Seed Extract is the extract of the seeds of the wheat, *Triticum monococcum*. [*Triticum monococcum* is also known as eikorn and is native to eastern Europe and western Asia].[12]	Skin-conditioning agent – misc.
Triticum Monococcum (Wheat) Stem Water	Triticum Monococcum (Wheat) Stem Water is the aqueous solution of the steam distillates obtained from the stems of *Triticum monococcum.*	Flavoring agent
Triticum Spelta Seed Water	Triticum Spelta Seed Water is the aqueous solution of the steam distillates obtained from the seeds of *Triticum spelta*.*	Skin-conditioning agent – misc.
Triticum Turgidum Durum (Wheat) Seed Extract	Triticum Turgidum Durum (Wheat) Seed Extract is the extract of the seeds of *Triticum turgidum durum*.	Skin-conditioning agent – misc.
Triticum Vulgare/Aestivum (Wheat) Grain Extract	Triticum Vulgare/Aestivum (Wheat) Grain Extract is the extract of the grains of *Triticum vulgare* and *Triticum aestivum*.	Hair conditioning agent; skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Bran	Triticum Vulgare (Wheat) Bran is the broken coat material of grains of wheat, *Triticum vulgare*.*	Abrasive; bulking agent
Triticum Vulgare (Wheat) Bran Extract 84012-44-2	Triticum Vulgare (Wheat) Bran Extract is the extract of the bran of *Triticum vulgare*.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Bran Lipids	Triticum Vulgare (Wheat) Bran Lipids is the cyclohexane extract of Triticum Vulgare (Wheat) Bran.*	Skin-conditioning agent - occlusive
Triticum Vulgare (Wheat) Flour Extract	Triticum Vulgare (Wheat) Flour Extract is the extract of the powder obtained by grinding wheat, *Triticum vulgare*.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Flour Lipids	Triticum Vulgare (Wheat) Flour Lipids is a mixture of lipids derived from the flour of *Triticum vulgare*.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Germ	Triticum Vulgare (Wheat) Germ is the natural product obtained from the embryo of the wheat kernel separated in milling.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Germ Extract 84012-44-2	Triticum Vulgare (Wheat) Germ Extract is the extract of the germ of *Triticum vulgare*.*	Skin bleaching agent; skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Germ Powder	Triticum Vulgare (Wheat) Germ Powder is the powder obtained from the dried, ground wheat germ, *Triticum vulgare*.*	Abrasive; absorbent; bulking agent; viscosity increasing agent - aqueous
Triticum Vulgare (Wheat) Germ Protein	Triticum Vulgare (Wheat) Germ Protein is a protein obtained from the germ of the wheat, *Triticum vulgare*.*	Hair conditioning agent; skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Gluten 8002-80-0	Triticum Vulgare (Wheat) Gluten is a protein substance which is intermixed with the starch portion in the endosperm of the wheat, *Triticum vulgare.**	Binder; hair conditioning agent; skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Gluten Extract	Triticum Vulgare (Wheat) Gluten Extract is the extract of Triticum Vulgare (Wheat) Gluten.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Kernel Flour	Triticum Vulgare (Wheat) Kernel Flour is the milled flour obtained from the finely ground kernels of wheat, *Triticum vulgare*.*	Abrasive; bulking agent; viscosity increasing agent - aqueous
Triticum Vulgare (Wheat) Protein	Triticum Vulgare (Wheat) Protein is a protein obtained from wheat, *Triticum vulgare*.*	Film former; hair conditioning agent; skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Seed Extract 84012-44-2	Triticum Vulgare (Wheat) Seed Extract is the extract of the seeds of *Triticum vulgare*.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Sprout Extract	Triticum Vulgare (Wheat) Sprout Extract is the extract of the young shoots of *Triticum vulgare*.*	Skin-conditioning agent – misc.
Triticum Vulgare (Wheat) Straw Water	Triticum Vulgare (Wheat) Straw Water is the aqueous solution of the steam distillates obtained from *Triticum vulgare* (wheat) straw.*	Skin-conditioning agent – misc.

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

Ingredient/CAS No.	Definition	Function
Wheat Germ Glycerides 68990-07-8	Wheat Germ Glycerides is a mixture of mono-, di-, and triglycerides produced by the transesterification of Triticum Vulgare (Wheat) Germ Oil.	Skin-conditioning agent - emollient

* The accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum*.[1]

Table 2. Generic plant part definitions as they apply to wheat-derived ingredients.[1]

Plant Part	Definition
Bran	The outer hard layers of the grain formed by the fused fruit and seed wall in grains and cereals.
Endosperm	Energy storage tissue inside seeds.
Germ	The embryo in a seed; the part of a seed that can develop into new plant.
Grain	Dry one-seeded fruits produced by grasses, e.g. cereals such as wheat.
Kernel	The grain of a grass.
Leaf	Flattened photosynthetic organs, attached to stems.
Pericarp	Fruit wall.
Seed	A propagating sexual structure resulting from the fertilization of an ovule, formed by embryo, endosperm, or seed coat.
Seed coat	Seed wall; testa; protective outer layer of seed, formed from the outer layers of the ovule
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.
Straw	The stem of a grass or related families

Table 3. Composition of 4 different Triticum Vulgare (Wheat) Bran Extract products[18]

Extract	Glycerin Extract	Propylene Glycol Extract	Propylene Glycol Extract	Soybean Oil Extract
Composition of Mixture	75%-100% glycerin 10%-25% water 5%-10% Triticum Vulgare (Wheat) Bran Extract	75%-100% propylene glycol 10%-25% Triticum Vulgare (Wheat) Bran Extract	95%-100% propylene glycol 1%-5% Triticum Vulgare (Wheat) Bran Extract	75%-100% soybean oil 10%-25% Triticum Vulgare (Wheat) Bran Extract
Solvent of Extraction	glycerin (vegetable origin)	1,2-propylene glycol	1,2-propylene glycol	soybean oil
Preservatives	0.35% potassium sorbate 0.35% sodium benzoate	0.35% potassium sorbate 0.35% sodium benzoate	0.35% potassium sorbate 0.35% sodium benzoate	none
Incidental Ingredients	0.1%-1% lactic acid	none	0.1%-1% lactic acid	none
Bacteriological Controls	100 germs/ml max.	100 germs/ml max.	100 germs/ml max.	100 germs/ml max.
Heavy Metals (solvent)	≤ 5 ppm total	not tested	not tested	not tested

Table 4. Frequency (2020) and concentration of use (2017, 2019) according to duration and type of exposure for *Triticum aestivum* (Wheat)-derived ingredients.[29-31]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Triticum Aestivum (Wheat) Flour Lipids		**Triticum Aestivum (Wheat) Germ Extract**		**Triticum Aestivum (Wheat) Seed Extract**		**Triticum Monococcum (Wheat) Seed Extract**	
Totals[†]	**17**	**NR**	**293**	**0.0002-0.6**	**166**	**NR**	**3**	**NR**
Duration of Use								
Leave-On	13	NR	247	0.0002-0.6	119	NR	2	NR
Rinse Off	4	NR	46	NR	46	NR	1	NR
Diluted for (Bath) Use	NR	NR	NR	NR	1	NR	NR	NR
Exposure Type								
Eye Area	1	NR	39	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	20	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 7[a]; 4[b]	NR	2; 74[a]; 71[b]	NR	7; 79[a]; 22[b]	NR	2[a]	NR
Incidental Inhalation-Powder	4[b]	NR	7; 71[b]	0.0002[c]	22[b]	NR	NR	NR
Dermal Contact	8	NR	251	0.0002-0.6	157	NR	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	9	NR	22	NR	9	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	22	NR	23	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Triticum Vulgare (Wheat) Bran[e]		**Triticum Vulgare (Wheat) Bran Extract[e]**		**Triticum Vulgare (Wheat) Bran Lipids[e]**		**Triticum Vulgare (Wheat) Flour Extract[e]**	
Totals[†]	**22**	**0.2-0.61**	**73**	**0.005-0.05**	**2**	**NR**	**2**	**NR**
Duration of Use								
Leave-On	20	NR	66	0.005-0.05	2	NR	NR	NR
Rinse Off	2	0.2-0.61	7	NR	NR	NR	2	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	2	NR	7	0.02	NR	NR	NR	NR
Incidental Ingestion	NR	NR	12	0.015	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]; 12[b]	NR	29[a]; 13[b]	0.02[a]	NR	NR	NR	NR
Incidental Inhalation-Powder	12[b]	NR	1; 13[b]	0.025-0.05[c]	NR	NR	NR	NR
Dermal Contact	21	0.2-0.61	59	0.005-0.05	NR	NR	2	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	2	0.01	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	2	0.2-0.61	13	0.015	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 4. Frequency (2020) and concentration of use (2017, 2019) according to duration and type of exposure for *Triticum aestivum* (Wheat)-derived ingredients.[29-31]

	# of Uses	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*	*# of Uses*	*Max Conc of Use (%)*
	Triticum Vulgare (Wheat) Flour Lipids[e]		**Triticum Vulgare (Wheat) Germ[e]**		**Triticum Vulgare (Wheat) Germ Extract***		**Triticum Vulgare (Wheat) Germ Protein[e]**	
Totals[†]	**NR**	**0.00065-0.1**	**5**	**NR**	**40**	**0.00001-13**	**60**	**0.0015-0.03**
Duration of Use								
Leave-On	NR	0.00065-0.1	4	NR	35	0.00001-13	12	0.0015-0.03
Rinse Off	NR	NR	1	NR	5	0.001-0.32	48	0.0075
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	0.00065	NR	NR	2	0.004-0.075	1	0.0075-0.01
Incidental Ingestion	NR	NR	NR	NR	NR	0.13	NR	NR
Incidental Inhalation-Spray	NR	0.05[a]	3[b]	NR	19[a]; 9[b]	0.005-0.32; 0.0012-0.025[a]; 0.02[b]	2[a]; 7[b]	NR
Incidental Inhalation-Powder	NR	0.1[c]	3[b]	NR	9[b]	13; 0.02[b]; 0.0001-0.2[c]	7[b]	0.015; 0.0075-0.03[c]
Dermal Contact	NR	0.05-0.1	5	NR	37	0.00001-13	13	0.0075-0.03
Deodorant (underarm)	NR	NR	NR	NR	NR	0.1-0.11[d]	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	2	0.001-0.32	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	46	NR
Nail	NR	NR	NR	NR	NR	NR	1	0.0015
Mucous Membrane	NR	NR	NR	NR	NR	0.1-0.13	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

	Triticum Vulgare (Wheat) Gluten Extract		**Triticum Vulgare (Wheat) Protein[e]**		**Triticum Vulgare (Wheat) Seed Extract**		**Triticum Vulgare (Wheat) Sprout Extract[e]**	
Totals[†]	**1**	**NR**	**93**	**0.01-0.16**	**NR**	**0.34**	**13**	**NR**
Duration of Use								
Leave-On	1	NR	76	0.01-0.16	NR	0.34	11	NR
Rinse Off	NR	NR	17	NR	NR	NR	2	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	16	0.16	NR	NR	1	NR
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NR	1; 7[a]; 34[b]	NR	NR	NR	2[a]; 5[b]	NR
Incidental Inhalation-Powder	NR	NR	34[b]	NR	NR	0.34[c]	5[b]; 2[c]	NR
Dermal Contact	NR	NR	76	0.16	NR	0.34	11	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	17	NR	NR	NR	1	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	1	NR
Nail	NR	NR	NR	0.01	NR	NR	NR	NR
Mucous Membrane	NR	NR	1	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	3	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 Wheat Germ Extract

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.

d. 0.11% in a spray deodorant

e. Listed with the nomenclature Triticum Aestivum in the VCRP database.

Table 5. Current and historical frequency and concentration according to duration and type of exposure for previously reviewed wheat-derived ingredients.[3,29,31]

	Triticum Vulgare (Wheat) Gluten*				Triticum Vulgare (Wheat) Kernel Flour*				Wheat Germ Glycerides			
	# of Uses		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*		*# of Uses*		*Max Conc of Use (%)*	
	2020	**2001**	**2019**	**2001**	**2020**	**2001**	**2019**	**2001**	**2020**	**2001**	**2019**	**2001**
Totals*	**21**	**5**	**0.0001-0.05**	**NR**	**4**	**NR**	**NR**	**NR**	**41**	**128**	**0.041-0.2**	**0.01-25**
Leave-On	6	4	0.001-0.05	NR	2	NR	NR	NR	37	128	0.041-0.2	0.05-25
Rinse-Off	15	1	0.0001-0.05	NR	2	NR	NR	NR	4	NR	NR	0.001
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Eye Area	NR	2	NR	NR	NR	NR	NR	NR	10	NR	0.041	0.05-2
Incidental Ingestion	NR	NR	NR	NR	NR	NR	NR	NR	3	126	NR	0.3-25
Incidental Inhalation-Spray	5[a]	NR	0.05	NR	1[b]	NR	NR	NR	7[a]; 14[b]	NR	NR	0.1[a]
Incidental Inhalation-Powder	NR	NR	NR	NR	1[b]	NR	NR	NR	14[b]	NR	0.2[c]	NR
Dermal Contact	2	3	0.001	NR	4	NR	NR	NR	34	1	0.041-0.2	0.05-2
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	19	NR	0.001-0.05	NR	NR	NR	NR	NR	4	NR	NR	0.001-0.1
Hair-Coloring	NR	NR	0.0001-0.0075	NR	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR	NR	1	NR	2
Mucous Membrane	NR	NR	NR	NR	1	NR	NR	NR	3	126	NR	0.3-25
Baby Products	NR	NR	0.001	NR	NR	NR	NR	NR	NR	NR	NR	NR

NR = Not reported

† Because each ingredient may be used in cosmetics with multiple exposure types, the sum of all exposure types may not equal the sum of total uses.

* Listed with the nomenclature Triticum Aestivum in the VCRP database.

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

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

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

Table 6. Ingredients not reported to be in use.[29,30]

Triticum Aestivum (Wheat) Leaf Extract
Triticum Aestivum (Wheat) Peptide
Triticum Monococcum (Wheat) Stem Water
Triticum Spelta Seed Water
Triticum Turgidum Durum (Wheat) Seed Extract
Triticum Vulgare/Aestivum (Wheat) Grain Extract
Triticum Vulgare (Wheat) Germ Powder
Triticum Vulgare (Wheat) Straw Water

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FINAL REPORT OF THE SAFETY ASSESSMENT FOR WHEAT FLOUR AND WHEAT STARCH

Wheat Flour, a natural product obtained from wheat grain, consists primarily of starch and gluten fractions. These ingredients are not toxic when administered orally. Dermatologic studies show these ingredients to be nonirritating and nonsensitizing.

Studies of allergic respiratory disorders caused by chronic inhalation of Wheat Flour dust are numerous, but the cosmetic use of this ingredient does not provide the conditions under which such sensitization is likely to occur.

Wheat Flour and Wheat Starch are safe as cosmetic ingredients in the present practices of use and concentration.

CHEMICAL AND PHYSICAL PROPERTIES

Preparation, Composition and Physical Characteristics

Wheat Flour Wheat Flour is the milled flour grain endosperm. It is a fine, soft powder that contains 70-75% carbohydrates, 9.5 - 13.5% protein (%N x 5.7), and approximately 12% moisture (CTFA, 1978a)[1].

The principal constituents of flour are starch and gluten, and their proportion varies greatly in different wheat varieties grown under different climatic conditions. The extremes have been reported to be, roughly, from 17% gluten and 70% starch to 6% gluten and 81% starch (Brother and Olcott, 1947).

The inorganic constituents of Wheat Flour are (in descending order): K(0.571%), P, S, Mg, Cl, Ca, Na, Si(0.006%). The elements Zn, Fe, Mn, B, Cu, and Al are present in concentrations no greater than 100 ppm (Sullivan, 1933).

There is abundant literature concerning the chemical and physical characteristics of Wheat Flour and its components (Agatova and Proskuryakov, 1962; Bietz and Wall, 1972; Bourdet, 1956; Boutaric and Fabry, 1945; Bungenberg de Jong and Klaar, 1929; Colvin and McCalla, 1949; DeRege, 1935; Dimler and Senti, 1959; Godon and Petit, 1967; Gortner, 1931; Grosskreutz 1961; Haex, 1962; Hoseney *et al.*, 1969; Howe, 1946; Hussein, 1961; Jones, 1961; Juvrud, 1927; Kaczkowski, 1965; Kimura, 1956; Lasztity, 1970; Laws and France, 1949; Lorenz and Maga, 1975; The Merck Index, 1976; Oh *et al.*, 1966; Pence *et al.*, 1950; Ponte *et al.*, 1967, Pradac, 1959; Prischep *et al.*, 1974a, b; Rohrlich, 1973; Sandstedt and Mattern, 1958; Stockelbach and Bailey, 1938; Wagner, 1948; Yakobenko and Litvinov, 1975).

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[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005

Wheat Starch Wheat Starch is the amylose and amylopectin-rich portion of Wheat Flour. It consists of 86-91% carbohydrates and 9-13% moisture (CTFA, 1978b).

Starch, a polymer of glucose, is the carbohydrate reserve of plants. Native starch occurs in minute granules varying in size and shape depending on the plant source. Starch molecules in the granule are held together by hydrogen bonding (Paschall 1974; Wurzburg, 1972).

The linear polymer amylose contains about 200 to 2,000 D-anhydroglucose units joined by alpha-1,4 bonds. The branched polymer amylopectin consists of linear alpha-1,4 linked segments branched through alpha-1,6 bonds at 15 to 25 anhydroglucose unit intervals (Paschall 1974; Wurzburg, 1972).

Wheat Starch is produced commercially by wet-milling processes in which the starch is liberated by grinding aqueous slurries of wheat grain. It is then refined, filtered, and dried. Sulfur dioxide is used to aid in the separation of starch from the protein matrix of wheat grain (Watson, 1967).

Reactivity

Wheat Flour Wheat flour contains no solvents or diluents (CTFA, 1978a). The water binding capacity of wheat flour is inversely related to pH and is not affected by iodate, N-ethylmaleimide, or sulfite, which affect the -SH -S-S system of flour proteins (Bushuk, 1963).

Flour proteins do not include papainases as formerly believed. The natural proteolytic enzymes of flour have marked effects on other proteins but have little, or no, action on flour proteins (Sandstedt and Mattern, 1958).

Wheat Starch Information is available regarding the many chemical treatments used in making modified starches as food ingredients (FASEB, 1977).

The water binding capacity of Wheat Starch is independent of pH (Bushuk, 1963.)

Gelatinization of Wheat Starch occurs with baking. This involves an irreversible crystallization of amylose. Parallelization of the amylose polymers and consequent association through hydrogen bonding occurs. The amylopectin fraction crystallizes slowly after cooling. This coacervation continues for several days (Wurzburg, 1972; Osman, 1967).

Amylose has an affinity for iodine, fatty acids, various surfactants, and other large molecules with hydrophobic and hydrophylic sections (Wurzburg, 1972).

Analytical Methods

The extensive literature on analytical methods for these ingredients is derived mostly from the milling and food technology industries (Laws and France, 1949, Anonymous, 1958; Bahl *et al.*, 1976; Benatar and Weneret, 1947; Benhamou-Glynn *et al.*, 1965; Berliner and Koopman, 1929; Berliner, 1939; Chabot, 1925; Cirilli, 1969; Eeckhaut, 1956; Hertwig, 1928; Jones *et al.*, 1963; Lawellin, 1920; Lawrence *et al.*, 1970; Libby, 1970; Marinelli,

1938; Morison, 1921; Pradac and Prugar, 1961; Rottinger and Woidich, 1928; Rottinger, 1929; Simskaya, 1951; Soenen and Pinguair, 1939; Stauffer *et al.*, 1958; Terent'eva *et al.*, 1973; Trop and Grossman, 1972; Ziegler, 1942).

Impurities

Wheat Flour The CTFA Cosmetic Ingredient Chemical Description for Wheat Flour includes the following as known minor impurities (CTFA, 1978a):

Sugars	1.5 to 2.0%
Fat	1.0 to 2.0%
Fiber (Cellulose)	0.35% maximum
Ash	0.3 to 0.8%

Wheat Flour contains no solvents or diluents (CTFA, 1978a). One study detected no nitrites or nitrosamines in Wheat Flour (Thewlis, 1967).

FDA rules permit the addition of certain materials in order to improve the nutritional value of Wheat Flour. As a result, much of the commercially available Wheat Flour is "enriched" with various vitamins and minerals. These may include niacin, riboflavin, thiamine, and iron (CTFA, 1978a).

Wheat Starch The CTFA Cosmetic Ingredient Chemical Description for Wheat Starch includes the following as known minor impurities (CTFA, 1978b):

Protein (%N x 6.25)	0.50% maximum
Fiber (Cellulose)	0.25% maximum
Ash	0.20% maximum
Fat (Ether Extractable)	0.15% maximum

Wheat Starch contains no diluents, solvents, or additives. Residual sulfur dioxide may be present at a concentration not greater than 0.008% (CTFA, 1978b).

USE

Cosmetic Use

Wheat Flour is found in one cleansing preparation, and Wheat Starch in four formulations of face powders. The concentrations and the associated number of product formulations for each of these ingredients are shown in Table 1 (FDA, 1976) below. The route and frequency of application of formulations containing these ingredients can only be inferred, but it is clear that the opportunity exists for eye contact and inhalation of small amounts as well as absorption through the skin. No information was available on possible interactions with other cosmetic ingredients, although wheat flour proteins have sulfhydryl and amino groups.

TABLE 1. Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product Formulations
Wheat Flour	Cleansing preparations (cold creams, cleansing lotions, liquids, pads)	>0.1 to 1	1
Wheat Starch	Face powders	> 10 to 25	2
		> 5 to 10	2

Wheat Starch is reported to have emollient and demulcent functions in cosmetic applications (Rinzler, 1977). It functions also as a carrier and absorbing agent in face powders.

Non-Cosmetic Use

Wheat Flour Wheat Flour has been a staple food for perhaps 10,000 years. It is currently used in breads, pastries, and pasta products and is usually baked before consumption.

Pursuant to the Food and Drug Administration, Wheat Flour is listed as a Generally Recognized as Safe (GRAS) food ingredient (21 CFR 137.105).

Wheat Starch Starch, mainly as a component of cereal products and vegetables, supplies about 20% of the energy content of the average American diet. The available food supply provides about 180 grams of starch per capita per day (Friend and Marston, 1975). In the food industry, unmodified starches are used primarily as thickening or gelling agents and processing aids. Dry granular starch is used as a diluent, bulking agent, fluidifying agent, and mold and moisture absorbing agent (Wurzburg, 1972; Osman, 1967).

Pursuant to the Food and Drug Administration, commercial Wheat Starch is listed as a Generally Recognized as Safe (GRAS) food ingredient (21 CFR 170.30(d)).

Non-food industrial applications of all unmodified starches account for another ten grams per capita per day (Russell, 1973). Gelatinized unmodified starch serves as an internal binder and sheet strengthener for paper products (Nissen, 1967). In the textile industry, starch is used primarily in the sizing of cotton yarns and is removed from most fabrics subsequent to weaving (Compton and Martin, 1967).

BIOLOGICAL PROPERTIES

General Effects

Wheat Flour is composed of a water-soluble fraction, starch (produced by water extraction), and a water-insoluble fraction, gluten (produced by water washing; not more than 17% yield). No evidence was available that suggests any biologically significant interaction between the two fractions. Thus, the

expected biological effects of Wheat Flour should be no more than the sum of the gluten and starch effects. Conversely, much of the data obtained for Wheat Starch or gluten can be logically linked to Wheat Flour.

Absorption, Metabolism, Storage and Excretion

Wheat Flour The rates and patterns of absorption of the gluten fraction of Wheat Flour across the intestinal wall in relation to celiac disease have been widely explored. Intestinal hydrolysis of gluten and absorption of the amino acids does not appear to be affected by the disease (Douglas and Booth, 1968; (1969). In addition, some research concerning the relationship between wheat exposure and fat and protein metabolisms indicates that gluten ingestion reduces liver cholesterol in the rat (Ranhotra, 1973, 1977; Ranhotra *et al.*, 1976) and decreases blood urea levels in human beings (Bolourchi, 1968).

Wheat Starch Rats have been found to absorb 23.2 g (standard deviation = 9.19) of starch per kg daily from a normal diet containing approximately 65% starch (Boyd, 1973). The intestinal absorption coefficient of starch for normal children 1-2 years old is greater than 99% (Auricchio *et al., 1967).*

Maltose, maltotriose, and alpha-limit dextrins containing five to nine glucose residues and one or more alpha-1,6 branching links are the products of alpha-amylase digestion of cooked (gelatinized) starch within the intestinal lumen. These products are then converted to glucose by an alpha-dextrinase, glucoamylase, and maltase contained in the intestinal mucosa brush border. Only glucose is transported through the intestinal wall into the bloodstream (Gray, 1975).

Animal Toxicity Studies

Acute Studies

Eye Irritation *Wheat Flour:* A mascara base containing the gluten fraction of Wheat Flour at a concentration of 1% was tested for eye irritation in rabbits by both the Draize procedure and that described in the Federal Hazardous Substances Act (CTFA, 1976). A mild circumcorneal injection was noted in 50% of the animals and a mild discharge in two animals. These changes were thought to be typical of those resulting from foreign objects in the eye and were attributed to mechanical effects of the dried mascara base. There was complete recovery within 72 hours.

Subchronic Studies

Wheat Flour It was observed in 1944 and confirmed in 1947 that wheat gluten flour at a level of 10% or higher in the diet produced "running fits" in dogs (canine hysteria) as early as three days after the start of the diet (Erickson *et al.*, 1947; Wagner and Elvehjem, 1944). Symptoms included epileptic seizures and running-barking episodes. It was subsequently shown that this disturbance was caused by a toxic factor produced by the interaction of wheat gluten with

the nitrogen trichloride used in the commerical processing of flour (Parry, 1948; Radomski *et al.*, 1948). Newell *et al.* (1948) later showed that high levels of NCl_3 treated wheat gluten in the diet are tolerated by several species of animals, including man. NCl_3 is no longer used in the processing of Wheat Flour.

Wheat Starch Wistar rats of 50 g initial body weight were fed, for 28 days, diets containing either six percent casein and 77% Wheat Starch or 15% casein and 66% Wheat Starch. The animals showed normal weight gains, protein efficiency ratios, and cecal weights (Reussner *et al.*, 1963).

A 90-day subchronic oral toxicity study was conducted with two groups of 20 rats each. One group received a diet containing 25% Wheat Starch by weight; the other was fed the basic stock diet. After 90 days, there were no significant differences in food consumption between the two groups and no differences in their hematology and urine analyses. There were no pathological findings (Hercules, 1961)

Clinical Assessment of Safety

Dermatologic Studies

Wheat Flour The Shelanski repeated insult patch test technique was used on 50 subjects to test two mascara base products each containing 1% wheat gluten. No adverse reactions occurred (CTFA, 1977a).

The Modified Draize-Shelanski repeated insult patch test technique was performed on 202 subjects using 1% wheat gluten in a mascara base. Of the 11 reactions that occurred, two were considered to be due to preservatives and nine to "non-specific irritation" (CTFA, 1977a).

One percent wheat gluten in a mascara base was worn by 50 subjects in normal usage under the supervision of a dermatologist. No objective signs of dermatitis were noted (CTFA, 1977b), but the duration of the study was not reported. During five years of use of two products containing wheat gluten, the number of reported adverse reactions was 2.0 for one product and 0.15 for the other product per 100,000 units sold. None of the reactions was attributed to wheat gluten (CTFA, 1977c).

Wheat Starch In a modified Draize repeated insult patch test performed on 23 human subjects, Wheat Starch was nonirritating and produced no sensitization (Hercules, 1959a).

Challenge reaction scores were obtained for 210 subjects in a Schwartz prophetic patch test using Wheat Starch moistened with distilled water. None of the 210 subjects exhibited signs of sensitization (Hercules, 1959b).

Ingestion Studies

Wheat Flour Herpetiformis and Celiac Disease: Dermatitis herpetiformis is a chronic, pruritic, papular-vescular eruption affecting extensor surfaces. An associated gluten-sensitive enteropathy, sometimes termed celiac disease or non-tropical sprue, occurs in approximately 65-95% of affected patients (Albot *et al.*, 1969; Allardyce and Shearman, 1975; Asquith, 1975; Auricchio, 1970;

Bataller *et al.*, 1973; Bender, 1974; Cornell and Townley, 1974; Dissanayake *et al.*, 1973; Evans and Patey, 1974; Ezeoke *et al.*, 1974; Falchuk and Strober, 1974; Fry *et al.*, 1974; Goldstein and Heiner, 1970; Hekkens *et al.*, 1972; Kasarda, 1972, 1975; Kendall *et al.*, 1972; Lancaster *et al.*, 1975; Laplane, 1972; Morganroth *et al.*, 1972; Rossipal and Palm, 1971; Schwob *et al.*, 1972; Seah *et al.*, 1972; Self *et al.*, 1969; Shmerling and Haring, 1971; Shmerling and Shiner, 1972; Strober *et al.*, 1975; Strumeyer and Fisher, 1972, 1973).

The pathogenesis of dermatitis herpetiformis is not fully understood. An immunologic mechanism is suggested by the finding of immunoglobulin A deposits in the dermal papillae of most affected patients (Katz and Strober, 1978; Marks and Shuster, 1970; Seah *et al.*, 1973; Van der Meer, 1969). Eterman *et al.* (1977), however, examined these IgA deposits and found no antibodies to wheat. More recent studies have demonstrated the presence of wheat specific IgG antibodies in sera from dermatitis herpetiformis and gluten-sensitive enteropathy patients (Huff *et al.*, 1979; Kavai *et al.*, 1977). Massey *et al.* (1977) have suggested that gluten entering the serum from a damaged intestinal mucosa forms an immune complex which activates the complement in the skin via the alternative pathway to cause an inflammatory reaction. The presence of IgA in such immune complexes has been reported (Zone and Provost, 1979).

Since the concentration of Wheat Flour in cosmetics is low (≤1%) and the proportion of the gluten fraction of Wheat Flour is no greater than 17% (net gluten concentration ≤.17%), there is little likelihood that enough wheat gluten could be absorbed by the percutaneous route or by inadvertent ingestion from cosmetic products containing Wheat Flour to precipitate a manifestation of either cutaneous or gastrointestinal symptoms.

Wheat Starch As much as two pounds of starch can be ingested per day by compulsive starch eaters (Allan and Woodruff, 1963; Merkatz, 1961; Silverman and Perkins, 1966; Warshauer, 1966). It is generally in the form of laundry starch, and on the basis of 14% moisture content, this provides 3160 calories. These people usually become obese and prone to iron-deficiency anemia; some have an enlargement of the parotid glands, and one patient, who consumed 3 to 4 pounds of starch per day, developed a starch gastrolith (Allan and Woodruff, 1963).

Inhalation Studies Studies of respiratory allergic disorders have focused on millers, bakers, and other people exposed chronically to flour dust (Baagoe, 1933; Beritic and Valic, 1971; Beritic and Zagar, 1972; Blands *et al.*, 1976; Castberg and Sorenson, 1948; Guibert *et al.*, 1963; Hendrick *et al.*, 1976; Herxheimer, 1967a, 1967b, 1973; Heyl *et al.*, 1970; Nakazawa *et al.*, 1972; Popa *et al.*, 1970; Schmidt, 1938; Schwartz, 1947; Valic and Stahuljak, 1971; Van Dishoeck and Roux, 1940, 1941; Van Vonno and Struycken, 1933; Woitowitz *et al.*, 1971a, b; Young, 1974). The evidence available indicates that flour hypersensitivity is acquired through chronic inhalation and an inherited allergic disposition. Wheat Flour contains 40 antigens, some showing partial immunological identity (Blands *et al.*, 1976). Symptoms of the disturbance include allergic asthma, chronic bronchitis, vasomotor rhinitis,

eczema, and skin hypersensitivity. The likelihood of skin sensitization (formation of antibody) increases with time (Herxheimer, 1967a, 1967b, 1973). The average time required for development of flour sensitization in bakers with chronic exposure was 10.8 years (Schwartz, 1947).

Since the concentration of Wheat Flour in cosmetics is low (≤1%) and the cleansing preparations containing flour offer little chance of chronic inhalation, acquisition of flour sensitive allergy through this route is extremely unlikely. Face powder formulations containing Wheat Starch afford a more obvious inhalation exposure potentiality; but in consideration of the experience with bakers and the lack of evidence that starch alone can cause allergy, there is little likelihood that Wheat Starch in cosmetic products could induce asthma.

SUMMARY

Wheat Flour, a natural product obtained from wheat grain, consists primarily of starch and gluten fractions. Wheat Flour is used at low concentrations (>0.1% to 1%) in one cleansing preparation, and Wheat Starch is used at concentrations up to 25% in four face powder formulations.

Since Wheat Flour is composed almost wholly of gluten and starch, the safety assessment of the flour is based essentially on the observations made in the testing and use of the gluten and starch separately. Practically no relevant toxicologic testing has been done directly on the flour itself.

These ingredients are not toxic when administered orally. Wheat products are digested and absorbed by the normal human gastrointestinal tract. Ingestion of up to two pounds of starch per day produced only obesity and iron-deficiency anemia in human beings. Immunologic reactions to wheat have been demonstrated and may play a role in the pathogenesis of dermatitis herpetiformis and gluten sensitive enteropathy, but it is unlikely that enough gluten could be ingested accidentally from cosmetic products containing Wheat Flour to elicit such reactions.

Dermatologic studies show these ingredients to be nonirritating and nonsensitizing.

Studies of allergic respiratory disorders caused by chronic inhalation of Wheat Flour dust are numerous, but the cosmetic use of this ingredient does not provide the conditions under which such sensitization is likely to occur.

CONCLUSIONS

On the basis of the available information presented herein, the Panel concludes that Wheat Flour and Wheat Starch are safe as cosmetic ingredients in the present practices of use and concentration.

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FINAL REPORT OF THE SAFETY ASSESSMENT FOR WHEAT GERM GLYCERIDES AND WHEAT GLUTEN

The results of tests on laboratory animals and humans for the safety of Wheat Germ Glycerides, Wheat Gluten, and of numerous cosmetic products containing these materials as presently used are reviewed.

These data support the conclusion that Wheat Germ Glycerides (0.25−2%) and Wheat Gluten (1%), in low concentrations in specific product formulations are non-sensitizing and non-irritating to human skin. Limited photopatch testing of Wheat Germ Glycerides in lipstick bases (1−2%) was also negative.

It is concluded that Wheat Germ Glycerides and Wheat Gluten are safe when incorporated in cosmetic products. They constitute no risk to the public as they are presently used in cosmetic products.

CHEMICAL AND PHYSICAL PROPERTIES

Preparation, Composition, and Physical Characteristics

Wheat Germ Glycerides Wheat germ, which is separated from the kernel by conventional milling processes, yields a light yellow or reddish-yellow oil. Transesterification of this wheat germ oil with glycerin forms Wheat Germ Glycerides. This ingredient contains 30 to 40% monoglycerides with di- and tri-glycerides of mixed fatty acids. For use in cosmetic formulations, the glycerides are mixed with 20 to 30% vegetable oils such as safflower oil and corn oil. About 0.05% BHT (butylated hydroxytoluene) and 0.25% di-alpha-tocopherol acetate are added as antioxidants. Details of the chemical composition of Wheat Germ Glycerides is given in Table 1.

TABLE 1. Chemical Composition and Impurities of Wheat Germ Glycerides (CTFA, 1978)[1]

Component Name	Range	Methods by Which Determined
Monoglyceride	30 — 40%	Periodic acid
Diglyceride	—	—
Glycerine	1.5% maximum	Periodic acid
Free fatty acids	0.7% maximum	—
Acid value	1.5 maximum	U.S.P.
Iodine value	110 minimum	Hanus
Acrolein	Negative	Colorimetric

[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005.

Wheat Gluten Wheat Gluten is the proteinaceous, sulfur-rich portion of wheat flour derived from the endosperm of the grain. It is prepared by water washing wheat flour then drying the insoluble matter with careful temperature control. The creamy-tan powder derived from this process is food grade and contains minor amounts of starch and fat (Agatova and Proskuryakov, 1962; CTFA, 1978[1]). Table 2 gives details of its composition.

TABLE 2. Chemical Composition and Impurities of Wheat Gluten (CFTA, 1978)[1]

Test	Range (% W/W)
Protein	75 minimum (moisture-free basis)
Fat	6.5
Moisture	5 — 7.5
Ash	1.0
Carbohydrates	
Starch	13.0
Reducing Sugars	0.5
Crude Fiber	0.5
Other	1.0

[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005.

Analytical Methods

The extensive literature on analytical methods applicable to Wheat Germ Glycerides and Wheat Gluten is derived primarily from the milling and food technology industries. These methods include procedures for determining individual components such as fatty acids or their glycerides, amino acids, and carbohydrates (Cah. Tech. Cent. Nat'l. Coord. Etud. Rech. Nutr. Aliment, 1958; Bahl *et al.*, 1976; Benetar and Weneret, 1947; Berliner, 1939; Berliner and Koopman, 1929; Benhamou-Glynn *et al.*, 1965; Chabot, 1925; Cirilli, 1969; Eeckhaut, 1956; Hertwig, 1928; Jones *et al.*, 1963; Lawellin, 1920; Lawrence *et al.*, 1970; Marinelli, 1938; Morison, 1921; Pradac and Prugar, 1961; Röttinger and Woidich, 1928; Röttinger, 1929; Soenen and Pinguair, 1939; Stauffer *et al.*, 1958; Terent'eva *et al.*, 1973).

USES

Wheat Germ Glycerides are used in over 200 cosmetic formulations, most commonly in lipsticks and moisturizers in concentrations ranging from less than 0.1 to 5%. Wheat Gluten is reportedly used in only one category, mascara, at 0.1% or less. The various types of cosmetics and the associated

[1]Available upon request. Administrator, Cosmetic Ingredient Review, Suite 212, 1133 15th St., NW, Washington, DC 20005.

concentration levels for Wheat Germ Glycerides and Wheat Gluten are shown in Table 3 (FDA, 1976). The route and frequency of application of cosmetic formulations containing these ingredients can only be inferred, but it is clear that the opportunity exists for eye contact, dermal absorption, and oral ingestion of small amounts. No information is available on possible interactions with other cosmetic ingredients, although Wheat Gluten contains reactive chemical groups such as sulfhydryl and amino groups.

TABLE 3. Product Formulation Data (FDA, 1976)

Ingredient	Cosmetic Product Type	Concentration (%)	Number of Product formulations
Wheat Germ Glycerides	Eye shadow	>0.1 to 1	3
	Other eye makeup preparations	>0.1 to 1	3
		≤0.1	1
	Face powders	>0.1 to 1	2
	Foundations	>0.1 to 1	8
		≤0.1	1
	Lipstick	>1 to 5	93
		>0.1 to 1	18
		≤0.1	3
	Makeup bases	>0.1 to 1	5
		≤0.1	1
	Cleansing (cold creams, cleansing lotions, liquids, and pads)	>0.1 to 1	7
		≤0.1	1
	Deodorants (underarm)	>0.1 to 1	1
	Face, body, and hand (excluding shaving preparations)	>1 to 5	1
		>0.1 to 1	11
	Hormone (creams, lotions)	>0.1 to 1	1
	Moisturizing (creams, lotions)	>0.1 to 1	21
		≤0.1	3
	Night (creams, lotions)	>1 to 5	1
		>0.1 to 1	9
		≤0.1	1
	Skin fresheners	≤0.1	1
	Wrinkle smoothing (removers)	≤0.1	1
	Other skin care preparations	>0.1 to 1	15
Wheat Gluten	Mascara	≤0.1	1

BIOLOGICAL PROPERTIES

Animal Toxicity Studies

Acute Studies

Oral Toxicity

Wheat Germ Glycerides In a single oral dose toxicity test of Wheat Germ Glycerides four groups of ten rats each received doses of 8, 16, 32, and 64 g/kg respectively. These doses resulted in one death on the second day after each of the two highest doses. These rats showed congestive changes in many organs and infectious lung conditions, but no effects specifically related to the test material. The surviving animals exhibited no adverse effects, and at the end of the 14-day observation period the average weight gain of those on the two highest doses was greater than that of the rats given the lower doses. From these observations, the LD 50 for Wheat Germ Glycerides would appear to be >64 g/kg (Calogero, 1959)[1].

Another single oral dose test of Wheat Germ Glycerides resulted in one death in ten rats on the 11th day after the lowest dose of 5 g/kg. Three higher doses reaching 14 g/kg, produced no deaths. These rats experienced diarrhea only during the first day at all dose levels. From these data the LD50 for Wheat Germ Glycerides would appear to be >14 g/kg (Calogero, 1977).

Wheat Germ Glycerides in Formulations Twelve formulations of lipstick frosteds, four of lipstick transparents, and four of blushers were each administered orally to groups of five male or five female Sprague-Dawley rats in a single dose of 5 g/kg or 5 ml/kg body weight. These formulations contained Wheat Germ Glycerides in concentrations ranging from 0.25 to 0.5% which are equivalent to doses of 12.5 to 25 ml/kg. No deaths occurred during any of these tests. The animals were observed for 14 days after treatment, but there was neither discussion of adverse symptoms nor any mention of their presence or absence. The procedures described in the Federal Hazardous Substances Act (FHSA) (16 CFR 1500) were followed: acute oral LD50 determinations were made only on test materials that produced deaths at doses of 5 mg/kg or 5 ml/kg (Calogero, 1977).

In a test of lipstick bases containing 1.2 to 2% Wheat Germ Glycerides, an oral dose of 25 g/kg caused no mortality in a group of 100 rats. Irritability and sluggishness immediately after dosing were attributed to the large volume of material administered. The animals were sacrificed and autopsied after 14 days. No gross abnormalities were reported (CTFA, 1976)[1].

Three skin treatment products containing 0.1% Wheat Germ Glycerides were each administered in single oral doses to rats and were reported to have LD50 values of >5 g/kg, >10 g/kg, and >10 g/kg, respectively (Calogero, 1976)[1].

Wheat Gluten A mascara base containing 1% Wheat Gluten was administered by gavage to 30 rats in a single dose of 25 mg/kg and to 40 rats in a

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dose of 50 g/kg. Two deaths at the lower dose and one at the higher dose occurred within 48 hours. The survivors generally showed irritability, diarrhea, and ataxia during the first 24 hours, with complete recovery in one week. After 14 days, autopsy findings in survivors were negative. The dead animals showed intestinal bloating or obstruction, probably due to the large volume of test material administered (CTFA, 1976)[1].

Eye Irritation

Wheat Germ Glycerides Two drops of undiluted Wheat Germ Glycerides in a rabbit eye produced minimal irritation of the conjunctiva in four of ten rabbits (the score 0.5 of a possible maximum of 110) when tested by the Draize method. This effect was observed in the first two days after a single application and disappeared on the third day. The highest average score was 0.3 (Kolmar Research Center, 1959).

In another study involving six rabbits, 0.1 ml of Wheat Germ Glycerides in the eye of six rabbits (Draize method) produced no irritation (Calogero, 1977)[1].

Wheat Germ Glycerides in Formulations Numerous formulations each of lipstick creams, frosteds, and transparents, and of blushers were tested for eye and mucosal surface irritation potential in groups of six rabbits each. The concentrations of Wheat Germ Glycerides in these products ranged from 0.25 to 0.50%. Evaluation of the effects on the cornea, iris, and conjunctiva, and of chemosis and discharge was done by the method of scoring for ocular lesions as described by Draize (1965). Four of the 12 lipstick creams and one of the four blushers showed low irritation indices. Two of the 12 lipstick creams tested scored 2 out of a possible score of 110. Of the 28 products studied, all others were scored zero (Calogero, 1977)[1].

In similar tests of a lipstick base at concentrations of 1.25 and 2.0% of Wheat Germ Glycerides on groups of 24 and 30 rabbits, respectively, no positive reactions were observed in any of the ocular parameters scored (CTFA, 1976)[1].

Three products containing 0.1% Wheat Germ Glycerides in a primary eye irritation test on rabbits produced transient minimal irritation of the conjunctiva in two cases and no irritation in the third (Calogero, 1975)[1].

Wheat Gluten A mascara base containing 1% Wheat Gluten was tested for eye irritation in rabbits by both the Draize procedure and the procedures required under FHSA. A mild circumcorneal injection was noted in 50% of the animals and a mild discharge in two animals. These changes were thought to be typical of those resulting from foreign objects in the eye and were attributed to drying of the mascara base. Complete recovery occurred within 72 hours (CTFA, 1976)[1].

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Skin Irritation

Wheat Germ Glycerides Different lots of Wheat Germ Glycerides were tested in rabbits for acute dermal toxicity by the Draize method and for primary dermal irritation using the procedures required under the Consumer Product Safety Act, 16 CFR 1500.3 (c) (4) and 1500.41. A mild irritation was observed especially on the abraded skin, but there was no evidence of systemic toxicity as reflected by food consumption or body weight. It was concluded that Wheat Germ Glycerides is not a primary irritant (Calogero, 1959, 1975, 1977)[1].

Other studies of cosmetic products containing Wheat Germ Glycerides, such as several lipstick preparations, liquid makeup, and others, revealed minimal skin irritation in a few of the test rabbits (Calogero, 1976; CTFA, 1976; Calogero, 1965)[1].

Guinea Pig Sensitization Sensitization by Wheat Germ Glycerides was evaluated in two groups of six guinea pigs each. One group received olive oil and the other a 0.1% solution of Wheat Germ Glycerides in olive oil. Initial injections were 0.05 ml intracutaneously. Subsequent injections of 0.1 ml were similarly given three times a week for a total of ten injections. Two weeks later a challenge injection of 0.05 ml was made. Observations were made on the days following the first and last injection. Mild reactions were observed in all animals except there was no reaction in one each of the control and experimental groups. Average scores for the experimental group were slightly less than for the controls indicating that Wheat Germ Glycerides is not a skin sensitizer in the guinea pig (Calogero, 1959)[1].

Subchronic Studies

Wheat Germ Glycerides A twelve-week feeding study was conducted on Wheat Germ Glycerides using weanling rats in three groups of five males and five females. They were given a basal diet supplemented with 1, 5 or 25% Wheat Germ Glycerides. An equal number of rats placed on the same basal diet (Rockland Rat Diet) served as controls. Two rats died: one male at four weeks in the control group and one female at 10 weeks in the 5% glycerides group. The results of observations on weight gain, efficiency of food utilization, hemoglobin, white and red blood cell counts, and liver and kidney weights as percents of body weights, all failed to show any evidence of adverse effects induced by the material under investigation. Numerous gross and histopathologic changes were found at the end of the feeding period but none of these was dose-related. The same lesions appeared in the controls and at the same rate of incidence as in the test animals. These data are tabulated in Table 4.

Wheat Gluten In 1944 it was observed that Wheat Gluten flour at a level of 10% or higher in the diet produced "running fits" in dogs (canine hysteria) as early as three days after the start of the diet (Wagner and Elvehjem, 1944). This condition was subsequently shown to be due to a toxic factor produced by the interaction of the Wheat Gluten with the nitrogen trichloride used in the

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TABLE 4 Rat Subchronic Feeding of Wheat Germ Glycerides (Calogero, 1959)[1]

Dietary Level	Number & Sex	12-Week Survivors	Weight Gain	Feed Efficiency gm/100 gm	Hemoglobin gm/100 ml	RBC $X10^{-6}$	WBC $X10^{-3}$	M/F Liver % Body Wt	M/F Kidney % Body Wt
None	5 M	4	205.2	11.2	14.8	6.5	21.5	3.9—5.9	1.1—2.6
	5F	5	154.3	6.2	14.0	6.0	12.2		
1%	5M	5	184.8	10.5	14.0	5.8	21.7	4.5—6.8	1.0—2.1
	5F	5	107.3	5.9	14.0	6.3	17.5		
5%	5M	5	172.1	10.2	12.8	6.0	18.2	3.9—5.6	1.3—2.1
	5F	4	139.3	6.6	12.8	5.6	13.4		
25%	5M	5	166.4	9.5	14.8	6.4	19.2	4.7—5.8	0.9—1.3
	5F	5	148.1	8.7	15.5	6.2	20.5		

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commercial processing of the flour (Erickson, *et al.*, 1947). This treatment of flour is no longer practiced. In a study by Newell *et al.*, (1949), it was shown that high levels of Wheat Gluten itself in the diet are tolerated by several species of animals, including human subjects.

CLINICAL ASSESSMENT OF SAFETY

Dermatologic Studies

Wheat Germ Glycerides Modified Draize-Shelanski repeated insult patch tests using 2% Wheat Germ Glycerides in a lipstick base were performed on 1154 subjects. Eight positive reactions occurred. These were mild and transitory and interpreted as non-specific irritant reactions by the investigating dermatologists who concluded that the product and/or ingredients caused no significant irritation (CTFA, 1977)[1].

Modified Draize-Shelanski repeated insult patch tests were performed on 200 subjects using three product formulations, each containing less than 0.1% Wheat Germ Glycerides. Test results indicated that the materials were considered to be non-irritating and non-sensitizing (Calogero, 1975)[1].

In another study using 0.25—0.5% Wheat Germ Glycerides in lipstick creams, lipstick frosteds, lipstick transparents, and blushers, the Modified Draize-Shelanski repeated insult patch test was performed on 150 subjects. No positive reactions occurred with lipstick creams, lipstick frosteds and blushers. There was one positive patch test (out of 150) with lipstick transparents. The investigators concluded that these products are non-irritating and non-sensitizing (Calogero, 1977)[1].

Schneider (1955)[1] tested patients with Wheat Germ Glycerides and concluded that 2% was non-irritating on healthy skin. Details of this study are lacking.

Five photopatch tests on 139 subjects using 2% Wheat Germ Glycerides in a lipstick base were performed and no significant reactions occurred. Photopatch testing of 24 subjects using 1% Wheat Germ Glycerides in lipstick caused no irritant or hypersensitivity reactions (CTFA, 1978, 1977)[1].

An in-use test of 149 subjects using 2% Wheat Germ Glycerides in a lipstick base under normal usage conditions resulted in no "untoward reactions" (CTFA, 1977)[1].

Wheat Gluten The Shelanski repeated insult patch test technique was used to test two mascara base products each containing 1% Wheat Gluten. Fifty subjects were employed and no adverse reactions occurred (CTFA, 1977)[1].

The modified Draize-Shelanski patch test was performed on 202 subjects using 1% Wheat Gluten in a mascara base. Eleven reactions occurred: two were considered to be due to preservatives and nine were considered "non-specific irritation" without further explanation (CTFA, 1977)[1].

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One percent Wheat Gluten in a mascara base was worn by subjects in normal usage under the supervision of a dermatologist. No objective signs of dermatitis were noted but the duration of the study was not reported (CTFA, 1977)[1].

Two products containing Wheat Gluten in use for five years were studied. The number of reactions per 100,000 sold was 2.0 for one product and 0.15 for the other product. None of the reactions was attributed to Wheat Gluten (CTFA, no date).

Dermatitis Herpetiformis is a chronic papular-vesicular eruption affecting all extensor surfaces. It is occasionally associated with small bowel disease resembling gluten-sensitive enteropathy, sometimes termed celiac disease or non-tropical sprue (Katz and Strober, 1978; Fry *et al.*, 1973; Marks and Whittle, 1969; Seah *et al.*, 1972).

The pathogenesis of Dermatitis Herpetiformis is not certain. An immunologic component is suggested by the finding of immunoglobulin A deposits in the dermal papillae in most patients (Katz and Strober, 1978; Van Der Meer, 1969; Seah *et al.*, 1973; Marks and Shuster, 1970). Eterman *et al.* (1977) examined these deposits but found no antibodies to wheat. However, Huff *et al.* (1979) have demonstrated circulating antibodies to wheat protein in Dermatitis Herpetiformis. Massey *et al.* (1977) have suggested that gluten entering the serum from a damaged intestinal mucosa forms an immune complex which activates complement in the skin via the alternate pathway thus causing an inflammatory reaction.

Since the concentration of gluten in cosmetics is low ($\leq 0.1\%$), there is no likelihood that enough Wheat 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.

SUMMARY

The results of tests on laboratory animals and humans for the safety of Wheat Germ Glycerides, Wheat Gluten, and of numerous cosmetic products containing these materials attest to the safety of these wheat products as presently used.

There are data supporting the conclusion that Wheat Germ Glycerides (0.25—2%) and Wheat Gluten (1%), in low concentrations in specific product formulations are non-sensitizing and non-irritating to human skin. Limited photopatch testing of Wheat Germ Glycerides in lipstick bases (1—2%) was also negative. Data from provocative or maximization testing of these individual materials in a wide range of concentrations are, however, lacking in human beings.

In tests on rats given single oral doses of these ingredients and of a limited number of their formulations, no LD50 values could be obtained because of the excessively large doses required. This illustrates the absence of significant acute systemic toxicity in these ingredients and their formulations and indi-

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cates a wide margin of safety should accidental oral ingestion occur. Subchronic feeding studies of high levels of Wheat Germ Glycerides and of Wheat Gluten in several species including human beings, provided further evidence that there is no risk from the use of these materials as cosmetic ingredients.

Numerous tests for eye and skin irritation in rabbits and skin tests in humans have shown only occasional minimal and rapidly reversible effects. No evidence of sensitization was observed in tests with the glycerides or the gluten.

The safety assessment of these ingredients rests on the information at hand and on the considerable usage in various concentrations in a variety of cosmetic formulations. Additional biological evaluation of these ingredients might reasonably be expected to incorporate more extended studies on the following:

1. Provocative or maximization patch testing on humans over a wide range of concentrations of both ingredients with observations for irritation, sensitization, photoirritation, and photosensitization.
2. Extension of the existing tests of both ingredients for dermal effects (as in 1 above) in humans at concentrations beyond the present data, for which the highest is 2%, to above 5% which is the maximum concentration reported in formulations.

CONCLUSIONS

On the basis of the information available, which the Expert Panel believes to be relevant and accumulated in a reasonable manner, the Panel concludes that Wheat Germ Glycerides and Wheat Gluten are safe when incorporated in cosmetic products and constitute no risk to the public in its present cosmetic use of these products.

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TABLE 31
Triticum Vulgare (Wheat) Gluten use

Product category	1976 use (Elder 1980a)	2001 use (FDA 2001)	1976 concentrations (Elder 1980a)	2001 concentrations (CTFA 2001)
Mascara	1	2	≤0.1%	—
Other shaving preparations	—	1	—	—
Other skin care preparations	—	2	—	—
Totals/ranges	1	5	≤0.1%	—

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WHEAT GERM GLYCERIDES AND WHEAT GLUTEN, WHEAT FLOUR AND WHEAT STARCH, AND WHEAT GERM OIL

Safety assessments of Wheat Germ Glycerides and Wheat Gluten were published in 1980 with the conclusion that these two ingredients were "safe when incorporated in cosmetic products and constitute no risk to the public in its present cosmetic use of these products" (Elder 1980a). Wheat Flour and Wheat Starch were found to be "safe as cosmetic ingredients in the present practices of use and concentration" (Elder 1980b). Wheat Germ Oil was also found "safe as a cosmetic ingredient in the present practices of use and concentration" (Elder 1980c). New studies, along with the updated information below regarding uses and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen these safety assessments.

TABLE 32
Triticum Vulgare (Wheat) Starch use

Product category	1976 use (Elder 1980b)	2001 use (FDA 2001)	1976 concentrations (Elder 1980b)	2001 concentrations (CTFA 2001)
Hair conditioners	—	1	—	0.01%–0.6%
Hair sprays (aerosol fixatives)	—	1	—	0.001%
Permanent waves	—	—	—	0.001%–0.2%
Shampoos (noncoloring)	—	—	—	0.001%–0.2%
Hair tonics, dressings, etc.	—	5	—	0.1%
Hair dyes and colors	—	19	—	—
Face powders	4	2	>5%–25%	0.1%
Foundations	—	—	—	3%
Bath soaps and detergents	—	—	—	25%
Skin cleansing preparations	—	1	—	0.03%
Face and neck skin care preparations	—	1	—	—
Body and hand skin care preparations	—	3	—	0.1%
Night skin preparations	—	1	—	—
Paste masks (mud packs)	—	4	—	—
Other skin care preparations	—	1	—	—
Totals/ranges	4	39	>5%–25%	0.001%–25%

TABLE 33
Triticum Vulgare (Wheat) Germ Oil

Product category (FDA 2001)	1976 use (Elder 1980c)	2001 use (FDA 2001)	1976 concentrations (Elder 1980c)	2001 concentrations (CTFA 2001)
Bath oils, tablets, and salts	2	—	>0.1%–5%	0.5%
Baby lotions, oils, powders, etc.	—	1	—	—
Bubble bath	1	—	≤0.1%	0.01%
Other bath preparations	—	1	—	0.001%–2%
Eyeliner	—	—	—	0.1%
Eye shadow	—	—	—	0.1%–3%
Eye lotion	2	—	≤0.1%–1%	0.2%–0.5%
Eye makeup remover	1	1	≤0.1%	—
Mascara	1	4	≤0.1%	0.5%
Other eye makeup preparations	—	4	—	0.00004%–0.5%
Colognes and toilet waters	—	—	—	0.01%
Hair Conditioner	7	26	≤0.1%–5%	0.0001%–1%
Hair Sprays (aerosol fixatives)	1	2	≤0.1	0.0002%–0.001%
Shampoos (noncoloring)	8	15	≤0.1%–1%	0.0001%–1%
Tonics, dressings, and other hair-grooming aids	—	19	—	0.001%–2%
Wave sets	4	—	≤0.1	0.0025%
Other hair preparations (noncoloring)	—	1	—	0.001%
Hair dyes and colors	—	7	—	0.1%
Hair shampoos (coloring)	1	—	≤0.1	—
Hair bleaches	—	5	—	—
Foundations	1	—	>0.1%–1%	—
Lipstick	21	33	≤0.1%–5%	0.1%–3%
Rouges	6	—	≤0.1%–1%	0.00005%
Other makeup preparations	—	—	—	0.5%–4%
Cuticle softeners	—	—	—	0.1%
Nail creams and lotions	1	2	>10%–15%	4%
Nail polish and enamel removers	1	2	>1%–5%	—
Bath soaps and detergents	—	3	—	0.02–1%
Deodorants	—	—	—	0.02%
Aftershave lotions	—	—	—	0.006%–2%
Beard Softeners	—	—	—	0.01%
Shaving cream (aerosol, brushless, and lather)	1	—	≤0.1%	0.006%
Other shaving preparations	1	1	>1%–5%	—
Skin cleansing preparations	8	13	≤0.1%–5%	0.00002%–5%
Depilatories	—	1	—	—
Face and neck skin care preparations[a]	5	19	>0.1%–5%	0.2%–10%
Body and hand skin care preparations[a]		31		0.001%–18%
Moisturizing preparations	17	37	≤0.1%–50%	0.001%–5%
Night preparations	5	14	≤0.1%–5%	0.5%–5%
Paste masks (mud packs)	1	8	>1%–5%	0.2%–2%
Skin fresheners	1	1	>1%–5%	8%
Other skin preparations	7	39	≤0.1%–25%	0.001%–1%
Suntan gels, creams, and liquids	4	7	>0.1%–5%	0.03%
Indoor tanning preparations	—	—	—	0.05%
Other suntan preparations	1	6	>0.1%–1%	—
Totals/ranges	113	303	≤0.1%–50%	0.00002%–18%

[a]Face and body skin care preparations were originally in the same category.

The Panel noted that a long history of reviewing plant-derived or "botanical" cosmetic ingredients has developed since these ingredients were first considered. As a result of that experience, it is now common to remind manufacturers that cosmetic products containing plant-derived ingredients should be formulated to limit the presence of pesticide/heavy metal residues as follows: lead ≤0.1 ppm; arsenic ≤3 ppm; mercury ≤1 ppm; total PCB/pesticide contamination ≤40 ppm, with ≤10 ppm for any specific residue (Andersen 1998).

The terminology for several of these ingredients in the *International Cosmetic Ingredient Dictionary and Handbook* has changed (Pepe, Wenninger, and McEwen 2002). Wheat Gluten is currently Triticum Vulgare (Wheat) Gluten. Wheat Flour is Triticum Vulgare (Wheat) Kernel Flour. Wheat Starch is Triticum Vulgare (Wheat) Starch. Wheat Germ Oil is Triticum Vulgare (Wheat) Germ Oil. The nomenclature for Wheat Germ Glycerides has not changed.

Wheat Germ Glycerides

Wheat Germ Glycerides were used in 212 formulations in 1976, primarily in lipsticks at concentrations up to 5%. In 2001, it was used in 128 products, 126 of which were lipsticks (FDA 2001), at concentrations up to 25% (CTFA 2001). Table 30 presents the available use information.

Triticum Vulgare (Wheat) Gluten

Triticum Vulgare (Wheat) Gluten was used in five formulations in 2001 (FDA 2001), as compared to one in 1976. No information on current use concentrations is given(CTFA 2001). Table 31 presents the available use information.

Triticum Vulgare (Wheat) Kernal Flour

Triticum Vulgare (Wheat) Kernal Flour was used in one formulation in 1976, in the concentration range of >0.1% to 1%. It was not reported to be used in cosmetics in 2001 (FDA 2001; CTFA 2001). No table is provided.

Triticum Vulgare (Wheat) Starch

Triticum Vulgare (Wheat) Starch was used in 39 formulations in 2001 (FDA 2001), as compared to 4 in 1976. Concentrations of use in 2001 (CTFA 2001) were at a maximum of 25%, the same as in 1976. Table 32 presents the available use information for Triticum Vulgare (Wheat) Starch.

Triticum Vulgare (Wheat) Germ Oil

Triticum Vulgare (Wheat) Germ Oil was reportedly used in 303 formulations in 2001 (FDA 2001), as compared to 113 in 1976. In 2001, the maximum concentration of use was 18% (CTFA 2001) compared to 50% in 1976. Table 33 presents the available use information.

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2020 FDA VCRP Raw Data

TRITICUM AESTIVUM (WHEAT) BRAN	03D	Eye Lotion	1
TRITICUM AESTIVUM (WHEAT) BRAN	03G	Other Eye Makeup Preparations	1
TRITICUM AESTIVUM (WHEAT) BRAN	05G	Tonics, Dressings, and Other Hair Grooming Aids	1
TRITICUM AESTIVUM (WHEAT) BRAN	07I	Other Makeup Preparations	1
TRITICUM AESTIVUM (WHEAT) BRAN	10A	Bath Soaps and Detergents	2
TRITICUM AESTIVUM (WHEAT) BRAN	12C	Face and Neck (exc shave)	7
TRITICUM AESTIVUM (WHEAT) BRAN	12D	Body and Hand (exc shave)	4
TRITICUM AESTIVUM (WHEAT) BRAN	12E	Foot Powders and Sprays	1
TRITICUM AESTIVUM (WHEAT) BRAN	12G	Night	2
TRITICUM AESTIVUM (WHEAT) BRAN	12J	Other Skin Care Preps	2
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	03D	Eye Lotion	4
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	03E	Eye Makeup Remover	1
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	03G	Other Eye Makeup Preparations	2
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	05A	Hair Conditioner	2
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	07B	Face Powders	1
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	07E	Lipstick	12
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	10E	Other Personal Cleanliness Products	1
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	11A	Aftershave Lotion	2
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12A	Cleansing	1
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12C	Face and Neck (exc shave)	10
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12D	Body and Hand (exc shave)	3
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12F	Moisturizing	23

TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12G	Night	4
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12H	Paste Masks (mud packs)	2
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12I	Skin Fresheners	1
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	12J	Other Skin Care Preps	3
TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	13B	Indoor Tanning Preparations	1
TRITICUM AESTIVUM (WHEAT) BRAN LIPIDS	05I	Other Hair Preparations	1
TRITICUM AESTIVUM (WHEAT) BRAN LIPIDS	12C	Face and Neck (exc shave)	1
TRITICUM AESTIVUM (WHEAT) FLOUR EXTRACT	12H	Paste Masks (mud packs)	2
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	03D	Eye Lotion	1
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	05A	Hair Conditioner	1
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	05B	Hair Spray (aerosol fixatives)	1
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	05F	Shampoos (non-coloring)	2
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	05G	Tonics, Dressings, and Other Hair Grooming Aids	5
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	12C	Face and Neck (exc shave)	4
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	12F	Moisturizing	1
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	12H	Paste Masks (mud packs)	1
TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	13B	Indoor Tanning Preparations	1

TRITICUM AESTIVUM (WHEAT) GERM	12A	Cleansing	1
TRITICUM AESTIVUM (WHEAT) GERM	12D	Body and Hand (exc shave)	3
TRITICUM AESTIVUM (WHEAT) GERM	12J	Other Skin Care Preps	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	03C	Eye Shadow	7
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	03D	Eye Lotion	23
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	03E	Eye Makeup Remover	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	03G	Other Eye Makeup Preparations	8
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	04E	Other Fragrance Preparation	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	05A	Hair Conditioner	14
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	05B	Hair Spray (aerosol fixatives)	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	05F	Shampoos (non-coloring)	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	05G	Tonics, Dressings, and Other Hair Grooming Aids	4
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	05I	Other Hair Preparations	2
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	07A	Blushers (all types)	4
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	07B	Face Powders	7
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	07C	Foundations	7
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	07E	Lipstick	20
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	07I	Other Makeup Preparations	4
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	10A	Bath Soaps and Detergents	1
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	10E	Other Personal Cleanliness Products	1

TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	11A	Aftershave Lotion	2
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	11G	Other Shaving Preparation Products	2
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12A	Cleansing	17
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12C	Face and Neck (exc shave)	56
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12D	Body and Hand (exc shave)	15
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12F	Moisturizing	49
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12G	Night	12
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12H	Paste Masks (mud packs)	9
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12I	Skin Fresheners	2
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	12J	Other Skin Care Preps	16
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	13B	Indoor Tanning Preparations	6
TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	13C	Other Suntan Preparations	1
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	03D	Eye Lotion	1
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	06A	Hair Dyes and Colors (all types requiring caution statements and patch tests)	44
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	06G	Hair Bleaches	2
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	08G	Other Manicuring Preparations	1
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	10E	Other Personal Cleanliness Products	1
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	12A	Cleansing	1
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	12C	Face and Neck (exc shave)	5

TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	12D	Body and Hand (exc shave)	2
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	12F	Moisturizing	2
TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	12J	Other Skin Care Preps	1
TRITICUM AESTIVUM (WHEAT) GLUTEN	05A	Hair Conditioner	5
TRITICUM AESTIVUM (WHEAT) GLUTEN	05F	Shampoos (non-coloring)	9
TRITICUM AESTIVUM (WHEAT) GLUTEN	05G	Tonics, Dressings, and Other Hair Grooming Aids	4
TRITICUM AESTIVUM (WHEAT) GLUTEN	05H	Wave Sets	1
TRITICUM AESTIVUM (WHEAT) GLUTEN	12F	Moisturizing	1
TRITICUM AESTIVUM (WHEAT) GLUTEN	12J	Other Skin Care Preps	1
TRITICUM AESTIVUM (WHEAT) GLUTEN EXTRACT	05I	Other Hair Preparations	1
TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	10A	Bath Soaps and Detergents	1
TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	12D	Body and Hand (exc shave)	1
TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	12H	Paste Masks (mud packs)	1
TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	12J	Other Skin Care Preps	1
TRITICUM AESTIVUM (WHEAT) PROTEIN	03D	Eye Lotion	5
TRITICUM AESTIVUM (WHEAT) PROTEIN	03G	Other Eye Makeup Preparations	11
TRITICUM AESTIVUM (WHEAT) PROTEIN	05A	Hair Conditioner	5
TRITICUM AESTIVUM (WHEAT) PROTEIN	05B	Hair Spray (aerosol fixatives)	1
TRITICUM AESTIVUM (WHEAT) PROTEIN	05F	Shampoos (non-coloring)	9
TRITICUM AESTIVUM (WHEAT) PROTEIN	05G	Tonics, Dressings, and Other Hair Grooming Aids	2
TRITICUM AESTIVUM (WHEAT) PROTEIN	07C	Foundations	11
TRITICUM AESTIVUM (WHEAT) PROTEIN	07I	Other Makeup Preparations	1

TRITICUM AESTIVUM (WHEAT) PROTEIN	10E	Other Personal Cleanliness Products	1
TRITICUM AESTIVUM (WHEAT) PROTEIN	12C	Face and Neck (exc shave)	28
TRITICUM AESTIVUM (WHEAT) PROTEIN	12D	Body and Hand (exc shave)	6
TRITICUM AESTIVUM (WHEAT) PROTEIN	12F	Moisturizing	4
TRITICUM AESTIVUM (WHEAT) PROTEIN	12G	Night	1
TRITICUM AESTIVUM (WHEAT) PROTEIN	12H	Paste Masks (mud packs)	2
TRITICUM AESTIVUM (WHEAT) PROTEIN	12J	Other Skin Care Preps	6
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	02D	Other Bath Preparations	1
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	04E	Other Fragrance Preparation	7
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	05A	Hair Conditioner	2
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	05C	Hair Straighteners	2
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	05D	Permanent Waves	2
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	05F	Shampoos (non-coloring)	1
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	05I	Other Hair Preparations	2
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	07I	Other Makeup Preparations	1
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	10A	Bath Soaps and Detergents	21
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	10E	Other Personal Cleanliness Products	1
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12A	Cleansing	17
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12C	Face and Neck (exc shave)	6
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12D	Body and Hand (exc shave)	16
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12F	Moisturizing	78

TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12G	Night	1
TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	12J	Other Skin Care Preps	8
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	01A	Baby Shampoos	1
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	01B	Baby Lotions, Oils, Powders, and Creams	2
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	03D	Eye Lotion	1
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	06H	Other Hair Coloring Preparation	1
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	07I	Other Makeup Preparations	1
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	12C	Face and Neck (exc shave)	5
TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	12F	Moisturizing	2
TRITICUM MONOCOCCUM (WHEAT) SEED EXTRACT	12A	Cleansing	1
TRITICUM MONOCOCCUM (WHEAT) SEED EXTRACT	12F	Moisturizing	2
WHEAT GERM EXTRACT	03D	Eye Lotion	1
WHEAT GERM EXTRACT	03F	Mascara	1
WHEAT GERM EXTRACT	05A	Hair Conditioner	1
WHEAT GERM EXTRACT	05F	Shampoos (non-coloring)	1
WHEAT GERM EXTRACT	07F	Makeup Bases	1
WHEAT GERM EXTRACT	11A	Aftershave Lotion	1
WHEAT GERM EXTRACT	11E	Shaving Cream	1
WHEAT GERM EXTRACT	12A	Cleansing	2
WHEAT GERM EXTRACT	12C	Face and Neck (exc shave)	6
WHEAT GERM EXTRACT	12D	Body and Hand (exc shave)	3
WHEAT GERM EXTRACT	12F	Moisturizing	15

WHEAT GERM EXTRACT	12I	Skin Fresheners	2
WHEAT GERM EXTRACT	12J	Other Skin Care Preps	3
WHEAT GERM EXTRACT	13A	Suntan Gels, Creams, and Liquids	1
WHEAT GERM EXTRACT	13C	Other Suntan Preparations	1

WHEAT GERM GLYCERIDES	03A	Eyebrow Pencil	2
WHEAT GERM GLYCERIDES	03B	Eyeliner	4
WHEAT GERM GLYCERIDES	03C	Eye Shadow	3
WHEAT GERM GLYCERIDES	03G	Other Eye Makeup Preparations	1
WHEAT GERM GLYCERIDES	05A	Hair Conditioner	1
WHEAT GERM GLYCERIDES	05F	Shampoos (non-coloring)	1
WHEAT GERM GLYCERIDES	05G	Tonics, Dressings, and Other Hair Grooming Aids	2
WHEAT GERM GLYCERIDES	07C	Foundations	2
WHEAT GERM GLYCERIDES	07E	Lipstick	3
WHEAT GERM GLYCERIDES	11A	Aftershave Lotion	1
WHEAT GERM GLYCERIDES	12A	Cleansing	2
WHEAT GERM GLYCERIDES	12C	Face and Neck (exc shave)	2
WHEAT GERM GLYCERIDES	12D	Body and Hand (exc shave)	12
WHEAT GERM GLYCERIDES	12F	Moisturizing	4
WHEAT GERM GLYCERIDES	12I	Skin Fresheners	1

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 27, 2020

SUBJECT: Triticum Vulgare (Wheat) Germ Extract

Anonymous. 2020. Method of manufacture Triticum Vulgare (Wheat) Germ Extract.

July 2020

Method of Manufacture Triticum Vulgare (Wheat) Germ Extract

Raw material: *Triticum vulgare* wheat germ

Solvent: Water

Wheat germ is solubilized in water. The insoluble material is removed and the extract is filtered.

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 3, 2020

SUBJECT: Triticum Vulgare (Wheat) Gluten

Kelisema srl. 2018. Gluplex LES Native wheat protein & Laurylether sulphate complex: Technical data sheet.

Anonymous. 2018. Summary of single insult patch test Gluplex LES (Triticum Vulgare (Wheat) Gluten and Sodium Laureth Sulfate).

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GLUPLEX LES

Native wheat protein & Laurylether sulphate complex

Identification	**INCI Name**	**CAS #**
	Triticum vulgare (Wheat) gluten	93384-22-6
	Sodium laureth sulfate	68891-38-3

Composition	**%**
Aqua	to 100
Triticum vulgare	4.7 - 6.4
Sodium laureth sulfate	7.0 - 8.0
Phenoxyethanol	< 1
Ethylparaben	< 1
Methylparaben	< 1

Description GLUPLEX LES is a solution of non-hydrolysed wheat gluten proteins in their original molecular size: solubility and stability are achieved by complexation with the anion lauryether sulphate. The complexation involves electrostatic and hydrophobic bonds which do not alter the primary and secondary structure of the protein macromolecules which are reversibly unfolded.

Appearance Clear yellow solution with low colour intensity and weak own odour.

Available types	**Liquid**	**Analytical methods**
Product code	P223123	
Specifications		
Residue on drying	12.0 - 15.0%	18h, 105 °C
Nitrogen content	0.8 - 1.1%	Kjeldahl
Protein content	4.7 - 6.4%	Kjeldahl
Ash	< 2%	6h, 600 °C
pH	5.0 - 6.0	Potentiometry
Microbial count	< 100 cfu/g	MM02
Mould and yeast	< 10 cfu/g	MM02
Typical data		
Laurylether sulphate	7.0 - 8.0%	

Preservatives Parabens in phenoxyethanol. Other preservative systems are available on request.

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Typical aminoacid composition (g/100g)	ASP	3,0	GLU	37,2	VAL	4,2
	LEU	6,9	ILE	3,8	PHE	5,2
	TYR	3,5	TRP	0,8	PRO	12,3
	MET	1,5	CYS	2,0	LYS	1,2
	ARG	2,8	HIS	2,2	GLY	3,1
	ALA	2,3	SER	4,8	THR	3,2

Molecular weight

The molecular weight of the complexed proteins ranges from few thousands to millions of Daltons.

Cosmetic properties

GLUPLEX LES is a vehicle for introducing in personal hygiene formulations non-hydrolysed, long chain wheat proteins, which are insoluble in the folded native form. This high molecular weight, high hydrophobic vegetable polymers show excellent protection against surfactant irritancy, confer smoothness to the skin and prevent swelling of the hair strand during detersion.

Miscibility and compatibility

GLUPLEX LES gives clear water solutions in the pH range from 5 to 8.
High ionic strength solutions can cause the opening of the complexation micelles with separation of re-folded proteins. (Precipitation with electrolytes is a identification test for native high molecular weight proteins). Full compatibility with anionic surfactants.
Compatible with amphoteric and nonionic surfactants.

Available technical documentation

The safety and applicative dossier on **GLUPLEX LES** includes the following technical documentation which is available upon request:

- **Tolerability tests:**
  - *Primary skin irritation test*
  - *In vitro ocular irritation test*
- **Efficacy tests:**
  - *Reduction of surfactant irritancy*
  - *Foaming properties*
- **Safety data sheet**

Uses

Mild detergents for skin and hair. Low irritating household detergents.

Suggested doses

2 to 10% in foam baths, liquid soaps, shower cleansers.
1 to 5% in shampoos.
1 to 5% in shave creams and gels.
1 to 5% in skinfriendly liquid dishwashers.

Storage and stability

GLUPLEX LES has to be stored in closed containers protected from heat. It can tolerate freezing without consequences for the complex stability. In the original unopened containers and suitable storage conditions the product is stable for at least six months.

Non-warranty

The information and recommendations in this data sheet are to the best of our knowledge reliable. Users should however make their own tests to determine the suitability of this product for their own particular purpose and to avoid the infringement of any patent.

Summary of Single Insult Patch Test – Gluplex – LES

(Triticum Vulgare (Wheat) Gluten [4.7-6.4%]; Sodium Laureth Sulfate [7-8%] – see technical data sheet for more information about composition)

Study completed in: 2018
Product tested as supplied (approximately 5% Triticum Vulgare (Wheat) Gluten)
Number of subjects tested: 20 (ages 19-62)
Application: to the upper back once (on day 1); under semi-occlusive patch (TruMed®) absorbent support in Webril® kept in position by a non-woven medical adhesive (surface 400 mm^2), quantity applied 160 µl
Exposure time: 48 ± 4 hours

Control: water was also applied to a skin area on the upper back under semi-occlusive patch during the 48-hour time period to take into account the possible effects not directly related to the investigation product but due to the patch material.

Skin examination: The skin was examined on day 1 before patching, on day 3, 15-30 minutes after patch removal and possible product removal, and on day 4, 24 hours after patch removal.

Results:

For the control area:

Control time after patch removal	Type of reaction	Number of reactive test subjects	% of reactive test subjects	Mean daily irritation score MDIS	Maximal mean irritation score MaxMIS
T15 / T30 minutes (D3)	None	0	0 %	0	0
T24h (D4)	None	0	0 %	0	

For the investigational product:

Control time after patch removal	Type of reaction	Number of reactive test subjects	% of reactive test subjects	Mean daily irritation score MDIS	Maximal mean irritation score MaxMIS	Skin compatibility of the product
T15 / T30 minutes (D3)	Very slight erythema	4	20 %	0,20	0,20	Good skin compatibility
T24h (D4)	Very slight erythema	4	20 %	0,20		

Conclusion: Under the experimental conditions (semi-occlusion, 48 hours), a single application of the product Gluplex LES induced no significant reaction of irritation and has a good skin compatibility.

Memorandum

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

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

DATE: July 17, 2020

SUBJECT: Tentative Report: Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics (Release Date: June 19, 2020)

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

Key Issue

Method of manufacture information is in the Method of Manufacture section of the tentative report for the following ingredients:

Triticum Vulgare (Wheat) Bran Extract (solvents: glycerin, propylene glycol, soybean oil)
Triticum Vulgare (Wheat) Kernel Flour
Triticum Vulgare (Wheat) Germ
Triticum Vulgare (Wheat) Gluten
Wheat Germ Glycerides

The *Dictionary* defines a "water" as the water soluble portion from a steam distillation". This information should be added to the Method of Manufacture section, and should be sufficient method of manufacture information for:

Triticum Monococcum (Wheat) Stem Water
Triticum Spelta Seed Water
Triticum Vulgare (Wheat) Straw Water

Method of manufacture information should not be needed for the following specific parts of wheat as they are prepared by separating one part of a wheat grain from the rest of the wheat grain as indicated in the ingredient definitions.

Triticum Vulgare (Wheat) Bran
Triticum Vulgare (Wheat) Germ Powder

Since the only information requested for these ingredients was method of manufacture, the above listed ingredients should be considered safe.

Additional Consideration

Composition/Impurities - What solvent system was used in the study described in reference 22?

Summary - Bran, not specifically wheat bran is an OTC laxative drug product.