Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics

Status:	Draft Report for Panel Review
Release Date:	August 22, 2019
Panel Meeting Date:	September 16-17, 2019

The 2019 Cosmetic Ingredient Review Expert Panel members are: Chair, Wilma F. Bergfeld, M.D., F.A.C.P.; Donald V. Belsito, M.D.; Curtis D. Klaassen, Ph.D.; Daniel C. Liebler, Ph.D.; James G. Marks, Jr., M.D., Ronald C. Shank, Ph.D.; Thomas J. Slaga, Ph.D.; and Paul W. Snyder, D.V.M., Ph.D. The CIR Executive Director is Bart Heldreth, Ph.D. This safety assessment was prepared by Christina L. Burnett, Senior Scientific Analyst/Writer.

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Memorandum

To: CIR Expert Panel Members and Liaisons
From: Christina L. Burnett, Senior Scientific Writer/Analyst
Date: August 22, 2019
Subject: Draft Safety Assessment on Wheat-Derived Ingredients

Enclosed is the Draft Report of the Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics. (It is identified as *wheat092019rep* in the pdf document.) The Scientific Literature Review (SLR) of these botanical ingredients was issued by CIR on June 19, 2019. Most of 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 agents, hair conditioning agents, and viscosity increasing agents. It should be noted that the accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum*; however, the *Dictionary* lists ingredients using all three nomenclatures.

This report includes three ingredients that have been previously reviewed and re-reviewed by the Panel: Triticum Vulgare (Wheat) Kernel Flour, Triticum Vulgare (Wheat) Gluten, and Wheat Germ Glycerides. These ingredients were found to be safe as used in cosmetic products; reports on these ingredients were originally published in 1980, and their safety was reaffirmed in a re-review that was published in 2003. Because it has been more than 15 years since the safety of these ingredients were last reviewed, these ingredients are included in this safety assessment for re-review.

The Council provided concentration of use survey data (*wheat092019data1; wheat092019data2*), human dermal irritation and sensitization data on Triticum Vulgare (Wheat) Germ Extract (*wheat092019data3),* and composition and method of manufacturing data on Triticum Vulgare (Wheat) Bran Extract (w*heat092019data4*). Comments on the SLR were received from the Council and addressed (*wheat092019pcpc*).

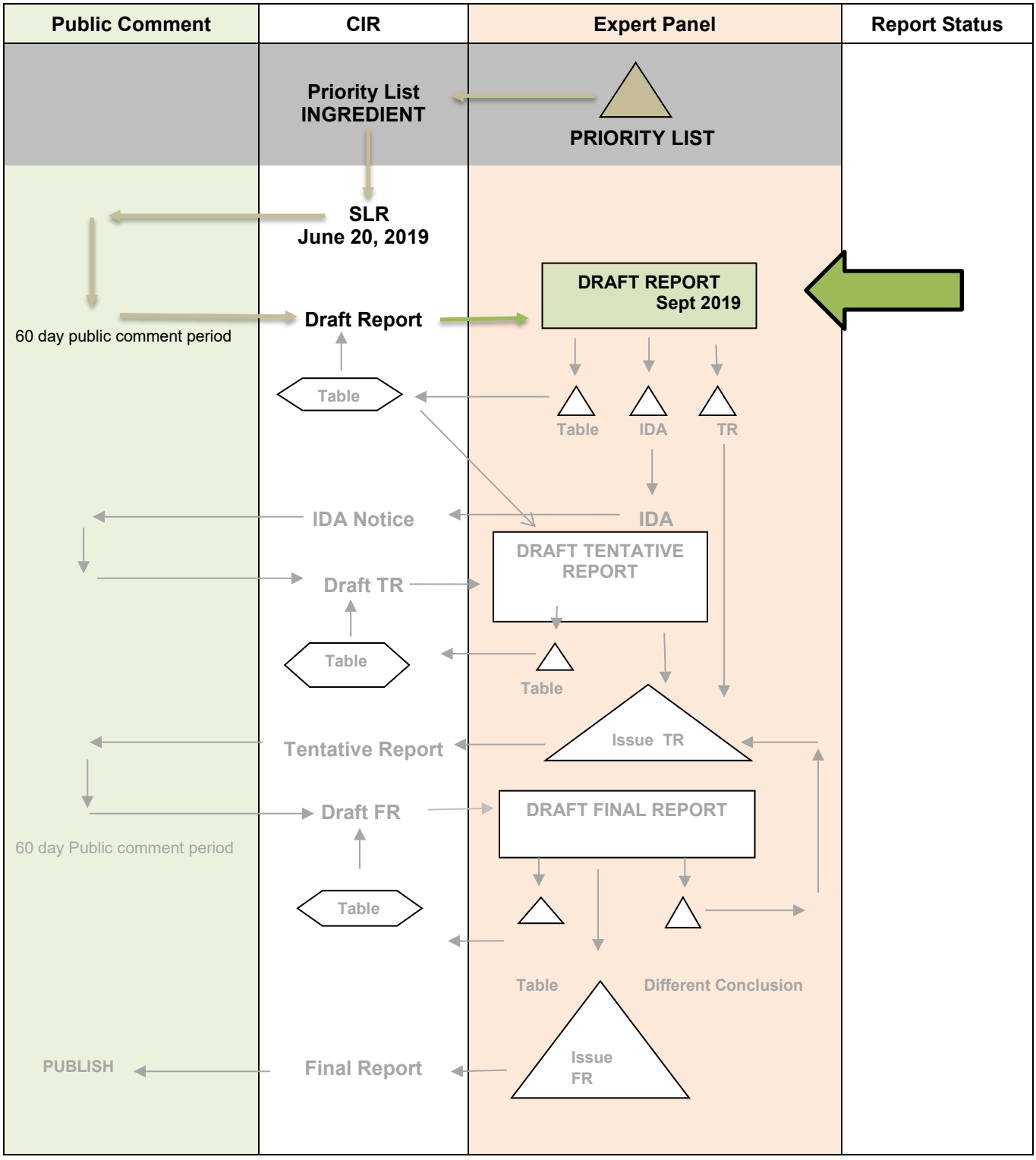
According to the 2019 VCRP survey data, Triticum Aestivum (Wheat) Germ Extract has the most reported uses in cosmetic products, with a total of 284 formulations; the majority of the uses are in leave-on skin care products. Triticum Aestivum (Wheat) Seed Extract has the second greatest reported number of uses in this safety assessment with 160 formulations; the majority of these 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 in 2017 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. 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. A concentration of use survey is currently being conducted on Triticum Spelta Seed Water; Triticum Vulgare (Wheat) Bran Lipids; Triticum Vulgare (Wheat) Gluten; Triticum Vulgare (Wheat) Gluten Extract; and Wheat Germ Glycerides.

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

SAFETY ASSESSMENT FLOW CHART

INGREDIENT/FAMILY Wheat-derived Ingredients

MEETING September 2019



Wheat-derived ingredients History

June 19, 2019 – Scientific Literature Review announced.

Wheat-Derived Ingredients, September 2019 – Christina Burnett

	Reported Use	GRAS	Method of Mfg	Constituents	Impurities	Toxico-kinetics		Acute Tox			Repeated Dose Tox			DART		Genotox		Carci		Dermal Irr.			Dermal Sens.			Photototoxicity	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 Aestivum (Wheat) Flour Lipids	X																												
Triticum Aestivum (Wheat) Germ Extract	X																												
Triticum Aestivum (Wheat) Leaf Extract				X																									
Triticum Aestivum (Wheat) Peptide																													
Triticum Aestivum (Wheat) Seed Extract	X																												
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) Flour Lipids	X																												
Triticum Vulgare (Wheat) Germ	X		X	X																									
Triticum Vulgare (Wheat) Germ Extract	X																							X					
Triticum Vulgare (Wheat) Germ Powder																													
Triticum Vulgare (Wheat) Germ Protein	X																												
Triticum Vulgare (Wheat) Gluten	X *	X	*																					*			*		

Wheat-Derived Ingredients, September 2019 – 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 Extract	X																												
Triticum Vulgare (Wheat) Kernel Flour	X		X	X	X																								
Triticum Vulgare (Wheat) Protein	X			X																									
Triticum Vulgare (Wheat) Seed Extract	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
Trticum 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

Typical Search Terms

- INCI names
- CAS numbers
- chemical/technical names
- additional terms will be used as appropriate

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)
- Scifinder (https://scifinder.cas.org/scifinder)

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

Fragrance Websites, if applicable

- IFRA (International Fragrance Association) – http://www.ifraorg.org/
- Research Institute for Fragrance Materials (RIFM) - http://rifm.org/

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INTRODUCTION

Most of 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, do not fall under the purview of the Cosmetic Ingredient Review (CIR). 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

The safety of Triticum Vulgare (Wheat) Kernel Flour was previously reviewed by the CIR Expert Panel (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 also 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 were 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 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 no 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 CIR typically evaluates, is provided on the CIR website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

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.

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.[11] *Triticum aestivum* L. is the most cultivated cereal grain in the world, making up about a third of total cereal grains. [12] *Triticum monococcum* is also known as eikorn and is native to eastern Europe and western Asia.[11] *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.[11,13] *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.[11,14] The accepted scientific name for both *Triticum vulgare* and *Triticum spelta* is *Triticum aestivum*.[1,13]

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.

Physical and 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.[12]

Method of Manufacture

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.

Triticum Vulgare (Wheat) Kernel Flour

Wheat flour is produced by different forms of milling or grinding, of the grain's endosperm.[12,19] The different forms of compression and shear allow for producing different grain sizes for different end uses or flour types.

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) 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.

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).[20] 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.[21]

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

A description of the composition of 4 different Triticum Vulgare (Wheat) Bran Extract products is 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.[22] 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).

There are four classes of protein in wheat flour: globulins, albumins, gliadins, and glutenins.[19] Gliadins and glutenins are components of gluten.

Triticum Vulgare (Wheat) Kernel Flour

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.[12] 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.[23] 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.[24] Further extraction with 90% acetone resulted in the precipitation of 70% glutathione. Phospholipid classes identified from hydroalcoholic extract of wheat sprouts included phosphatidylethanol-amine, phosphatidylcholine, phosphatidic acid, phosphatidylinositol, and lysophosphatidylcholine.[25] 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 tri-glycerides 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 the 2019 VCRP survey data, Triticum Aestivum (Wheat) Germ Extract has the most reported uses in cosmetic products with a total of 284 formulations; the majority of the uses are in leave-on skin care products (Table 4).[26] Triticum Aestivum (Wheat) Seed Extract has the second greatest reported number of uses in this safety assessment with 160 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 in 2017 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.[27] 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, Wheat Germ Glycerides has the most reported uses according to 2019 VCRP data with 40 (36 of which are in leave-on products); 128 uses (mostly in lipsticks) were reported in 2001 (Table 5).[3,26] The maximum concentration of use range for Wheat Germ Glycerides in 2001 was 0.001% to 25%, with 25% reported in lipsticks.[3] A concentration of use survey on the previously reviewed ingredients is currently being conducted by the Council for this safety assessment, and those data will be added once they are received. 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%.[27]

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.[27] 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.[28,29] 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.[30,31] 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.[30] 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.[27] 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.[32-34]

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.[35]

Non-Cosmetic

The FDA requires allergen labeling when major allergens, such as wheat, are included in food.[36] 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.[37] It has been investigated for anti-inflammatory properties.

Bran (source not specified) is an over-the-counter (OTC) laxative drug product.[38] 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.[17,39] Wheat sprout extract has been studied for its antioxidant content and potential use as a food ingredient and in cancer treatments.[24,25,40] 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.[41]

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 addressed in this safety assessment are found in the foods we consume daily. The potential for systemic effects, other than sensitization, from the possible absorption of these ingredients through the skin is much less than the potential for systemic effects 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.[42] 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, 10 mice received 70 ml, and 6 mice received 140 ml, in 18 equal doses by gavage) starting 3 days before the B[a]P treatment. Twenty-eight mice received just B[a]P. The sperm of the treated mice were examined 5 weeks 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

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.[43] 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.[43] 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.[44] 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

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).[42] 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.[42] 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 days (0.1 ml/day) 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

Co-Carcinogenicity

Triticum Vulgare (Wheat) Bran

In a 31-week 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.[45] 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 weeks. 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 weeks. The control group (12 rats) received a fiber-free diet throughout the 31 weeks. 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 Vulgare (Wheat) Sprout Extract

The effects of wheatgrass extract on skin papillomagenesis induced by DMBA and croton oil were investigated in male Swiss albino mice.[46] 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 two weeks later by croton oil (1% in 100 µl acetone) three times a week for a total of 16 weeks; Group 2 (pre-group) received wheatgrass leaf extract orally (20 ml/kg bw) for 7 days 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 days prior to receiving the croton oil, as in Group1; 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 seven days 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.

The tumorigenic effects of wheat sprout extract (S-30 fraction) were investigated using 8-week-old male BALB/c mice.[42] 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 weeks. 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 weeks without the croton oil promoter during both the initiator and promoter phases (n = 13). Wheat sprout extract, when injected subcutaneously for 10 days during carcinogenesis initiation in mice, shortened the latency period from 9 to 4 weeks 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 weeks. 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.

IRRITATION AND SENSITIZATION

Dermal Irritation

Animal

Wheat Germ Glycerides

Mild irritation was observed on abraded rabbit skin following dermal application of different lots of Wheat Germ Glycerides (concentrations not provided).[4] Minimal skin irritation was observed in rabbits that received dermal applications of Wheat Germ Glycerides in several different cosmetic formulations.

Dermal Sensitization

Animal

Wheat Germ Glycerides

Wheat Germ Glycerdies (0.1% solution in olive oil) was not a dermal sensitizer in a guinea pig sensitization study.[4]

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.[47] The test material (200 mg) was applied to the test sites as supplied. The patches were partially occlusive and 2 cm^2 in area. No irritation or sensitization was observed.

Triticum Vulgare (Wheat) Gluten and Wheat Germ Glycerides

Formulations containing up to 1% Triticum Vulgare (Wheat) Gluten and up to 2% Wheat Germ Glycerides were not dermal irritants or sensitizers in HRIPTs or in in-use studies.[4]

Ocular Irritation Studies

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.

OCCUPATIONAL EXPOSURES

Work-related sensitization (IgE mediated) to wheat flour and grain dusts has been reported in bakery workers.[48-50] Symptoms typically include rhinitis and asthma and other respiratory symptoms, but may also include contact urticaria and hand eczema. Skin-prick testing, skin biopsies, and radioallergosorbent tests (RAST) have been utilized to identify and analyze the reactions observed in bakery workers.

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, do not fall under the purview of the CIR.

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 2019 VCRP survey data, Triticum Aestivum (Wheat) Germ Extract has the most reported uses in cosmetic products with a total of 284 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 160 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. Triticum Vulgare (Wheat) Kernel Flour has 4 reported uses in 2019; no uses were reported in 2001. The concentration of use in 2001 was reported as a range > 0.1% to 1%; a concentration of use survey has not yet been conducted by Council for this safety assessment.

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. Wheat bran is an OTC laxative drug product, and wheat germ is an OTC weight control 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 addressed in this safety assessment are found in the foods consumed daily the world over. The potential for systemic effects, other than sensitization, from the possible absorption of these ingredient through the skin is much less than the potential for systemic effects 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.

Sperm abnormalities were not observed in mice that received wheat sprout extract (40 - 140 ml) orally, and sperm abnormalities were decreased in mice that received the extract with simultaneous treatment of B[a]P.

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/day) and DMBA.

Tumor incidences were increased in a 31-week study of rats that received a dietary supplement containing 20% wheat bran during administration of a carcinogen for 13 weeks 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-week 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.

Work-related sensitization has been reported in bakery workers. Symptoms include rhinitis, asthma, contact urticaria, and hand eczema.

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

DISCUSSION

To be determined.

CONCLUSION

To be determined.

TABLES

Table 1. Definitions and functions of the ingredients in this safety assessment.[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].[11]	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.

Ingredient/CAS No.	Definition	Function
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.
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)	$\leq$ 5 ppm total	not tested	not tested	not tested

Table 4. Frequency (2019) and concentration of use (2017) according to duration and type of exposure for *Triticum aestivum* (Wheat)-derived ingredients[26,27]

	# 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†	**16**	**NR**	**284**	**0.0002-0.6**	**160**	**NR**	**3**	**NR**
Duration of Use								
Leave-On	12	NR	240	0.0002-0.6	115	NR	2	NR
Rinse Off	4	NR	44	NR	44	NR	1	NR
Diluted for (Bath) Use	NR	NR	NR	NR	1	NR	NR	NR
Exposure Type								
Eye Area	NR	NR	39	NR	NR	NR	NR	NR
Incidental Ingestion	NR	NR	18	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	1; 7[a]; 4[b]	NR	2; 71[a]; 70[b]	NR	7; 78[a]; 22[b]	NR	2[a]	NR
Incidental Inhalation-Powder	4[b]	NR	7; 70[b]	0.0002[c]	22[b]	NR	NR	NR
Dermal Contact	7	NR	246	0.0002-0.6	151	NR	3	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	9	NR	20	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	20	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†	**21**	**0.2-0.61**	**69**	**0.005-0.05**	**2**	**NS**	**2**	NR
Duration of Use								
Leave-On	20	NR	62	0.005-0.05	2	NS	NR	NR
Rinse Off	1	0.2-0.61	7	NR	NR	NS	2	NR
Diluted for (Bath) Use	NR	NR	NR	NR	NR	NS	NR	NR
Exposure Type								
Eye Area	2	NR	7	0.02	NR	NS	NR	NR
Incidental Ingestion	NR	NR	10	0.015	NR	NS	NR	NR
Incidental Inhalation-Spray	3[a]; 12[b]	NR	28[a]; 12[b]	0.02[a]	NR	NS	NR	NR
Incidental Inhalation-Powder	12[b]	NR	1; 12[b]	0.025-0.05[c]	NR	NS	NR	NR
Dermal Contact	20	0.2-0.61	57	0.005-0.05	NR	NS	2	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NS	NR	NR
Hair - Non-Coloring	1	NR	2	0.01	NR	NS	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NS	NR	NR
Nail	NR	NR	NR	NR	NR	NS	NR	NR
Mucous Membrane	1	0.2-0.61	11	0.015	NR	NS	NR	NR
Baby Products	NR	NR	NR	NR	NR	NS	NR	NR

	# 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**		**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) Kernel Flour[e]**		**Triticum Vulgare (Wheat) Protein[e]**		**Triticum Vulgare (Wheat) Seed Extract**	
Totals[†]	**1**	**NS**	**4**	**NS**	**95**	**0.01-0.16**	**NR**	**0.34**
Duration of Use								
Leave-On	1	NS	2	NS	78	0.01-0.16	NR	0.34
Rinse Off	NR	NS	2	NS	17	NR	NR	NR
Diluted for (Bath) Use	NR	NS	NR	NS	NR	NR	NR	NR
Exposure Type								
Eye Area	NR	NS	NR	NS	17	0.16	NR	NR
Incidental Ingestion	NR	NS	NR	NS	NR	NR	NR	NR
Incidental Inhalation-Spray	NR	NS	1[b]	NS	1; 7[a]; 35[b]	NR	NR	NR
Incidental Inhalation-Powder	NR	NS	1[b]	NS	35[b]	NR	NR	0.34[c]
Dermal Contact	NR	NS	4	NS	77	0.16	NR	0.34
Deodorant (underarm)	NR	NS	NR	NS	NR	NR	NR	NR
Hair - Non-Coloring	1	NS	NR	NS	17	NR	NR	NR
Hair-Coloring	NR	NS	NR	NS	NR	NR	NR	NR
Nail	NR	NS	NR	NS	NR	0.01	NR	NR
Mucous Membrane	NR	NS	1	NS	1	NR	NR	NR
Baby Products	NR	NS	NR	NS	NR	NR	NR	NR

	# of Uses	*Max Conc of Use (%)*
	Triticum Vulgare (Wheat) Sprout Extract[e]	
Totals[†]	13	NR
Duration of Use		
Leave-On	11	NR
Rinse Off	2	NR
Diluted for (Bath) Use	NR	NR
Exposure Type		
Eye Area	1	NR
Incidental Ingestion	NR	NR
Incidental Inhalation-Spray	2[a]; 5[b]	NR
Incidental Inhalation-Powder	5[b]; 2[c]	NR
Dermal Contact	11	NR
Deodorant (underarm)	NR	NR
Hair - Non-Coloring	1	NR
Hair-Coloring	1	NR
Nail	NR	NR
Mucous Membrane	NR	NR
Baby Products	3	NR

NR = Not reported; NS = Not yet surveyed

† 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[3,26]

	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 (%)*	
	2019	**2001**	**2019**	**2001**	**2019**	**2001**	**2019**	**2001**	**2019**	**2001**	**2019**	**2001**
Totals*	**21**	**5**	**NS**	**NR**	**4**	**NR**	**NS**	**NR**	**40**	**128**	**NS**	**0.01-25**
Leave-On	6	4	NS	NR	2	NR	NS	NR	36	128	NS	0.05-25
Rinse-Off	15	1	NS	NR	2	NR	NS	NR	4	NR	NS	0.001
Diluted for (Bath) Use	NR	NR	NS	NR	NR	NR	NS	NR	NR	NR	NS	NR
Eye Area	NR	2	NS	NR	NR	NR	NS	NR	9	NR	NS	0.05-2
Incidental Ingestion	NR	NR	NS	NR	NR	NR	NS	NR	3	126	NS	0.3-25
Incidental Inhalation-Spray	5[a]	NR	NS	NR	1[b]	NR	NS	NR	7[a]; 14[b]	NR	NS	0.1[a]
Incidental Inhalation-Powder	NR	NR	NS	NR	1[b]	NR	NS	NR	14[b]	NR	NS	NR
Dermal Contact	2	3	NS	NR	4	NR	NS	NR	33	1	NS	0.05-2
Deodorant (underarm)	NR	NR	NS	NR	NR	NR	NS	NR	NR	NR	NS	NR
Hair - Non-Coloring	19	NR	NS	NR	NR	NR	NS	NR	4	NR	NS	0.001-0.1
Hair-Coloring	NR	NR	NS	NR	NR	NR	NS	NR	NR	NR	NS	NR
Nail	NR	NR	NS	NR	NR	NR	NS	NR	NR	1	NS	2
Mucous Membrane	NR	NR	NS	NR	1	NR	NS	NR	3	126	NS	0.3-25
Baby Products	NR	NR	NS	NR	NR	NR	NS	NR	NR	NR	NS	NR

NR = Not reported; NS = Not yet surveyed

† 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.

Table 6. Ingredients not reported to be in use.[26,27]

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

*Concentration of use not yet surveyed by the Council.

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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

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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

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

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

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

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

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		

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

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

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-

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

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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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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Annual Review of Cosmetic Ingredient Safety Assessments—2001/2002[1]

The Cosmetic Ingredient Review (CIR) Expert Panel has assessed the safety of over 1100 cosmetic ingredients since its inception in 1976. The very first safety assessments were published in earlier incarnations of this journal—the *Journal of Environmental Pathology and Toxicology* in 1980, and the *Journal of the American College of Toxicology* from 1982 to 1996.

Because information relevant to the safety of ingredients may have become available since these early safety assessments were published, the CIR Expert Panel has initiated a re-review process. If new information is thought to be available or if a long period of time has passed, the CIR Expert Panel may initiate a search for relevant new data.

In some cases, newly available data are largely redundant with the data available in the original safety assessment. In other cases, there is new safety data. If after considering any newly available information, the CIR Expert Panel decides not to reopen a safety assessment, this finding, along with any background material, is summarized and announced publicly. To assure that the scientific community is aware of any new information and the decision not to reopen, this *Annual Review of Cosmetic Ingredient Safety Assessments* is prepared. This is the first such annual review.

For each original safety assessment, the re-review addresses the import of new studies that were considered by the CIR Expert Panel, if any were available. A reference list is provided that updates the references provided in the original safety assessment. The re-review also captures information on the industry's current practices of ingredient use, updating the data available in the earlier report. Although this material provides the opinion of the CIR Expert Panel regarding the new data described, it does not constitute a full safety review.

The ingredients the CIR Expert Panel considered through June of 2002 and decided not to reopen are:

Aluminum Distearate
Aluminum Stearate
Aluminum Tristearate
Ammonium Stearate
Avocado Oil (aka Persea Gratissima (Avocado) Oil)
Calcium Stearate
Caprylic/Capric Triglyceride
Carbomers
Decyl Oleate
Glycol Stearate
Glycol Stearate SE
Glycol Distearate
Imidazolidinyl Urea
Isodecyl Oleate
Isopropyl Lanolate
Lithium Stearate
Magnesium Stearate
Potassium Stearate
Quaternium-18
Quaternium-18 Hectorite
Quaternium-18 Bentonite
Sodium Stearate
Squalene
Squalane
Stearalkonium Chloride
Wheat Germ Glycerides
Wheat Gluten (*aka* Triticum Vulgare (Wheat) Gluten)
Wheat Flour (*aka* Triticum Vulgare (Wheat) Kernel Flour)
Wheat Starch (*aka* Triticum Vulgare (Wheat) Starch)
Wheat Germ Oil (*aka* Triticum Vulgare (Wheat) Germ Oil)
Zinc Stearate

AVOCADO OIL (*aka* PERSEA GRATISSIMA (AVOCADO) OIL)

A safety assessment of Avocado Oil was published in 1980 with the conclusion "safe for use as presently incorporated into cosmetic formulations" (Elder 1980). Studies available since that safety assessment was completed, along with the updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

The CIR Expert Panel discussion focused on the new studies reporting the co-occurrence of latex and avocado allergies. Because the oil derived from the avocado has no protein component, Persea Gratissima (Avocado) Oil used in cosmetics is not expected to cross-react in individuals who are allergic to latex.

The Panel noted that a long history of reviewing plant-derived or "botanical" cosmetic ingredients has developed since these

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TABLE 30
Wheat Germ Glycerides use

Product category	1976 use (Elder 1980a)	2001 use (FDA 2001)	1976 concentrations (Elder 1980a)	2001 concentrations (CTFA 2001)
Eyeliner	—	—	—	0.05%–2%
Eye shadow	3	—	>0.1%–1%	2%
Other eye makeup preparations	4	—	≤0.1%–1%	—
Hair conditioners	—	—	—	0.001%
Hair tonics, dressings, etc.	—	—	—	0.1%
Face powders	2	—	>0.1%–1%	—
Foundations	9	—	≤0.1%–1%	2%
Lipstick	114	126	≤0.1%–5%	0.3%–25%
Makeup bases	6	—	≤0.1%–1%	—
Other makeup preparations	—	1	—	0.3%
Cuticle softeners	—	1	—	2%
Deodorants (underarm)	1	—	>0.1%–1%	—
Aftershave lotions	—	—	—	0.4%
Cleansing preparations (cold creams, cleansing lotions, liquids, and pads)	8	—	≤0.1%–1%	—
Face and neck skin care preparations[a]	12	—	>0.1%–5%	—
Body and hand skin care preparations[a]		—		—
Hormone (creams, lotions)[b]	1	—	>0.1%–1%	—
Moisturizing preparations[c]	24	—	≤0.1%–1%	—
Wrinkle smoothing (removers)[c]	1	—	≤0.1%	—
Night (creams, lotions)	11	—	≤0.1%–5%	—
Skin fresheners	1	—	≤0.1%	—
Other skin care preparations	15	—	>0.1%–1%	—
Totals/ranges	212	128	≤0.1%–5%	0.001%–25%

[a]Originally, Face and Neck and Body and Hand were combined as one category, but now they are separated.
[b]No longer a product category.
[c]Wrinkle smoothing (removers) are now part of the Moisturizing category.

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STEARALKONIUM CHLORIDE

A safety assessment of Stearalkonium Chloride was published in 1982 with the conclusion that this ingredient is "safe when incorporated in cosmetic products in concentrations similar to those presently marketed" (Elder 1982). New studies, along with the updated information regarding uses and use concentrations, were considered by the CIR Expert Panel. The Panel determined to not reopen this safety assessment.

In 1976, Stearalkonium Chloride was used in 249 cosmetic products, with the largest single use in rinses (noncoloring) in the concentration range of >0.1% to 5%. In 2001, Stearalkonium Chloride was used in 151 products (FDA 2001), with the largest single use reported for hair conditioners. The highest concentration of use was also in hair conditioners (0.7% to 7%) in 2001 (CTFA 2001). Table 29 presents the available use information.

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[2]Available from Director, Cosmetic Ingredient Review, 1101 17th Street NW, Suite 310, Washington, DC 20036, USA.

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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2019 VCRP RAW DATA

03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) BRAN	1
03G - Other Eye Makeup Preparations	TRITICUM AESTIVUM (WHEAT) BRAN	1
05G - Tonics, Dressings, and Other Hair Grooming Aids	TRITICUM AESTIVUM (WHEAT) BRAN	1
07I - Other Makeup Preparations	TRITICUM AESTIVUM (WHEAT) BRAN	1
10A - Bath Soaps and Detergents	TRITICUM AESTIVUM (WHEAT) BRAN	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) BRAN	7
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) BRAN	4
12E - Foot Powders and Sprays	TRITICUM AESTIVUM (WHEAT) BRAN	1
12G - Night	TRITICUM AESTIVUM (WHEAT) BRAN	2
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) BRAN	2

03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	4
03E - Eye Makeup Remover	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
03G - Other Eye Makeup Preparations	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	2
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	2
07B - Face Powders	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
07E - Lipstick	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	10
10E - Other Personal Cleanliness Products	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
11A - Aftershave Lotion	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	2
12A - Cleansing	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	9
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	3
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	22
12G - Night	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	4
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	2
12I - Skin Fresheners	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	3

13B - Indoor Tanning Preparations	TRITICUM AESTIVUM (WHEAT) BRAN EXTRACT	1
05I - Other Hair Preparations	TRITICUM AESTIVUM (WHEAT) BRAN LIPIDS	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) BRAN LIPIDS	1
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) FLOUR EXTRACT	2
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	1
05B - Hair Spray (aerosol fixatives)	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	1
05F - Shampoos (non-coloring)	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	2
05G - Tonics, Dressings, and Other Hair Grooming Aids	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	5
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	4
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	1
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	1
13B - Indoor Tanning Preparations	TRITICUM AESTIVUM (WHEAT) FLOUR LIPIDS	1
12A - Cleansing	TRITICUM AESTIVUM (WHEAT) GERM	1
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) GERM	3
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) GERM	1
03C - Eye Shadow	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	7
03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	23
03E - Eye Makeup Remover	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
03G - Other Eye Makeup Preparations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	8
04E - Other Fragrance Preparation	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	13
05B - Hair Spray (aerosol fixatives)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
05F - Shampoos (non-coloring)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1

05G - Tonics, Dressings, and Other Hair Grooming Aids	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	3
05I - Other Hair Preparations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	2
07A - Blushers (all types)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	4
07B - Face Powders	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	7
07C - Foundations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	7
07E - Lipstick	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	18
07I - Other Makeup Preparations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	3
10A - Bath Soaps and Detergents	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
10E - Other Personal Cleanliness Products	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
11A - Aftershave Lotion	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	2
11G - Other Shaving Preparation Products	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	2
12A - Cleansing	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	16
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	56
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	14
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	48
12G - Night	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	11
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	9
12I - Skin Fresheners	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	2
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	16
13B - Indoor Tanning Preparations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	6
13C - Other Suntan Preparations	TRITICUM AESTIVUM (WHEAT) GERM EXTRACT	1
03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	1
06A - Hair Dyes and Colors (all types requiring caution statements and patch tests)	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	44
06G - Hair Bleaches	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	2
08G - Other Manicuring Preparations	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	1

10E - Other Personal Cleanliness Products	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	1
12A - Cleansing	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	5
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	2
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	2
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) GERM PROTEIN	1
10A - Bath Soaps and Detergents	TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	1
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	1
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	1
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) KERNEL FLOUR	1
03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) PROTEIN	5
03F - Mascara	TRITICUM AESTIVUM (WHEAT) PROTEIN	1
03G - Other Eye Makeup Preparations	TRITICUM AESTIVUM (WHEAT) PROTEIN	11
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) PROTEIN	5
05B - Hair Spray (aerosol fixatives)	TRITICUM AESTIVUM (WHEAT) PROTEIN	1
05F - Shampoos (non-coloring)	TRITICUM AESTIVUM (WHEAT) PROTEIN	9
05G - Tonics, Dressings, and Other Hair Grooming Aids	TRITICUM AESTIVUM (WHEAT) PROTEIN	2
07C - Foundations	TRITICUM AESTIVUM (WHEAT) PROTEIN	11
07I - Other Makeup Preparations	TRITICUM AESTIVUM (WHEAT) PROTEIN	1
10E - Other Personal Cleanliness Products	TRITICUM AESTIVUM (WHEAT) PROTEIN	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) PROTEIN	28
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) PROTEIN	7
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) PROTEIN	4
12G - Night	TRITICUM AESTIVUM (WHEAT) PROTEIN	1
12H - Paste Masks (mud packs)	TRITICUM AESTIVUM (WHEAT) PROTEIN	2
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) PROTEIN	6

02D - Other Bath Preparations	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	1
04E - Other Fragrance Preparation	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	7
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	2
05C - Hair Straighteners	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	2
05D - Permanent Waves	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	2
05F - Shampoos (non-coloring)	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	1
05I - Other Hair Preparations	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	2
07I - Other Makeup Preparations	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	1
10A - Bath Soaps and Detergents	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	21
10E - Other Personal Cleanliness Products	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	1
12A - Cleansing	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	15
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	6
12D - Body and Hand (exc shave)	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	16
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	77
12G - Night	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	1
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) SEED EXTRACT	5
01A - Baby Shampoos	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	1
01B - Baby Lotions, Oils, Powders, and Creams	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	2
03D - Eye Lotion	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	1
06H - Other Hair Coloring Preparation	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	1
07I - Other Makeup Preparations	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	1
12C - Face and Neck (exc shave)	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	5
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) SPROUT EXTRACT	2
12A - Cleansing	TRITICUM MONOCOCCUM (WHEAT) SEED EXTRACT	1

12F - Moisturizing	TRITICUM MONOCOCCUM (WHEAT) SEED EXTRACT	2
03D - Eye Lotion	WHEAT GERM EXTRACT	1
03F - Mascara	WHEAT GERM EXTRACT	1
05A - Hair Conditioner	WHEAT GERM EXTRACT	1
05F - Shampoos (non-coloring)	WHEAT GERM EXTRACT	1
07F - Makeup Bases	WHEAT GERM EXTRACT	1
11A - Aftershave Lotion	WHEAT GERM EXTRACT	1
11E - Shaving Cream	WHEAT GERM EXTRACT	1
12A - Cleansing	WHEAT GERM EXTRACT	2
12C - Face and Neck (exc shave)	WHEAT GERM EXTRACT	6
12D - Body and Hand (exc shave)	WHEAT GERM EXTRACT	3
12F - Moisturizing	WHEAT GERM EXTRACT	15
12I - Skin Fresheners	WHEAT GERM EXTRACT	2
12J - Other Skin Care Preps	WHEAT GERM EXTRACT	3
13A - Suntan Gels, Creams, and Liquids	WHEAT GERM EXTRACT	1
13C - Other Suntan Preparations	WHEAT GERM EXTRACT	1
05I - Other Hair Preparations	TRITICUM AESTIVUM (WHEAT) GLUTEN EXTRACT	1
05A - Hair Conditioner	TRITICUM AESTIVUM (WHEAT) GLUTEN	5
05F - Shampoos (non-coloring)	TRITICUM AESTIVUM (WHEAT) GLUTEN	9
05G - Tonics, Dressings, and Other Hair Grooming Aids	TRITICUM AESTIVUM (WHEAT) GLUTEN	4
05H - Wave Sets	TRITICUM AESTIVUM (WHEAT) GLUTEN	1
12F - Moisturizing	TRITICUM AESTIVUM (WHEAT) GLUTEN	1
12J - Other Skin Care Preps	TRITICUM AESTIVUM (WHEAT) GLUTEN	1

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

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D., Executive Director
COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: October 2, 2017

SUBJECT: Concentration of Use by FDA Product Category: Wheat-Derived Ingredients

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

Triticum Vulgare (Wheat) Germ Extract
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 Turgidum Durum (Wheat) Seed Extract
Triticum Vulgare/Aestivum (Wheat) Grain Extract
Triticum Vulgare (Wheat) Bran
Triticum Vulgare (Wheat) Bran Extract
Triticum Vulgare (Wheat) Flour Extract
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
Triticum Vulgare (Wheat) Sprout Extract
Triticum Vulgare (Wheat) Straw Water

Ingredient	Product Category	Maximum Concentration of Use
Triticum Vulgare (Wheat) Germ Extract	Eye shadows	0.075%
Triticum Vulgare (Wheat) Germ Extract	Eye lotions	0.004-0.05%
Triticum Vulgare (Wheat) Germ Extract	Hair conditioners	0.004-0.32%
Triticum Vulgare (Wheat) Germ Extract	Hair sprays Aerosol	 0.005-0.32%
Triticum Vulgare (Wheat) Germ Extract	Shampoos (noncoloring)	0.001%
Triticum Vulgare (Wheat) Germ Extract	Tonics, dressings and other hair grooming aids	0.025%
Triticum Vulgare (Wheat) Germ Extract	Blushers	0.00001%
Triticum Vulgare (Wheat) Germ Extract	Face powders	13%
Triticum Vulgare (Wheat) Germ Extract	Foundations	0.13%
Triticum Vulgare (Wheat) Germ Extract	Lipstick	0.13%
Triticum Vulgare (Wheat) Germ Extract	Bath soaps and detergents	0.1%
Triticum Vulgare (Wheat) Germ Extract	Deodorants Not spray Aerosol	 0.1% 0.11%
Triticum Vulgare (Wheat) Germ Extract	Aftershave lotions	0.0019%
Triticum Vulgare (Wheat) Germ Extract	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0012-0.02%
Triticum Vulgare (Wheat) Germ Extract	Face and neck products Not spray	 0.012-0.2%
Triticum Vulgare (Wheat) Germ Extract	Body and hand products Not spray	 0.0001-0.02%
Triticum Vulgare (Wheat) Germ Extract	Moisturizing products Not spray	 0.02-0.1%
Triticum Vulgare (Wheat) Germ Extract	Foot powders and sprays	0.02%
Triticum Vulgare (Wheat) Germ Extract	Moisturizing products Not spray	 0.02-0.1%
Triticum Vulgare (Wheat) Germ Extract	Paste masks and mud packs	0.02-0.3%
Triticum Vulgare (Wheat) Germ Extract	Skin fresheners	0.0012%

Triticum Vulgare (Wheat) Germ Extract	Other skin care preparations	0.006-0.014%
Triticum Vulgare (Wheat) Germ Extract	Suntan products Not spray	0.05%
Triticum Vulgare (Wheat) Germ Extract	Indoor tanning preparations	0.02%
Triticum Vulgare (Wheat) Germ Extract	Other suntan preparations	0.02%
Triticum Aestivum (Wheat) Germ Extract	Face and neck products Not spray	0.0002%
Triticum Aestivum (Wheat) Germ Extract	Other skin care preparations	0.6%
Triticum Vulgare (Wheat) Bran	Bath soaps and detergents	0.2%
Triticum Vulgare (Wheat) Bran	Other personal cleanliness products	0.61%
Triticum Vulgare (Wheat) Bran Extract	Eye lotions	0.02%
Triticum Vulgare (Wheat) Bran Extract	Tonics, dressings and other hair grooming aids Not spray	0.01%
Triticum Vulgare (Wheat) Bran Extract	Foundations	0.005%
Triticum Vulgare (Wheat) Bran Extract	Lipstick	0.015%
Triticum Vulgare (Wheat) Bran Extract	Aftershave lotions	0.01%
Triticum Vulgare (Wheat) Bran Extract	Face and neck products Not spray	0.05%
Triticum Vulgare (Wheat) Bran Extract	Body and hand products Not spray	0.025%
Triticum Vulgare (Wheat) Bran Extract	Suntan products Not spray	0.01%
Triticum Vulgare (Wheat) Bran Extract	Indoor tanning preparations	0.02%
Triticum Vulgare (Wheat) Flour Lipids	Mascara	0.00065%
Triticum Vulgare (Wheat) Flour Lipids	Face and neck products Not spray	0.1%
Triticum Vulgare (Wheat) Flour Lipids	Indoor tanning preparations	0.05%
Triticum Vulgare (Wheat) Germ Protein	Mascara	0.01%
Triticum Vulgare (Wheat) Germ Protein	Other eye makeup preparations	0.0075%
Triticum Vulgare (Wheat) Germ Protein	Powders (dusting and talcum)	0.015%
Triticum Vulgare (Wheat) Germ Protein	Other manicuring preparations	0.0015%
Triticum Vulgare (Wheat) Germ Protein	Skin cleansing (cold creams, cleansing lotions, liquids and pads)	0.0075%
Triticum Vulgare (Wheat) Germ Protein	Face and neck products Not spray	0.0075%
Triticum Vulgare (Wheat) Germ Protein	Body and hand products Not spray	0.03%
Triticum Vulgare (Wheat) Protein	Eye lotions	0.16%
Triticum Vulgare (Wheat) Protein	Nail polish and enamel	0.01%
Triticum Vulgare (Wheat) Seed Extract	Face and neck products Not spray	0.34%

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

Information collected in 2017
Table prepared: October 2, 2017

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

TO: Bart Heldreth, Ph.D.
Executive Director - COSMETIC INGREDIENT REVIEW (CIR)

FROM: Beth A. Jonas, Ph.D.
Industry Liaison to the CIR Expert Panel

DATE: October 2, 2017

SUBJECT: Triticum Vulgare (Wheat) Germ Extract

Product Investigations, Inc. 2010. Determination of the irritating and sensitizing propensities of a face and body powder (containing 13% Triticum Vulgare (Wheat) Germ Extract) on human skin.

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

PRODUCT INVESTIGATIONS, INC.

151 East Tenth Avenue
Conshohocken, PA 19428
610-825-5855 • fax 610-825-7288

[redacted]

DETERMINATION OF THE IRRITATING AND SENSITIZING PROPENSITIES OF [redacted] ON HUMAN SKIN

Face and body powder containing 13% Triticum Vulgare (wheat) Germ Extract

PREPARED FOR

[redacted]

31 August 2010

[redacted]

TABLE OF CONTENTS

DETERMINATION OF THE IRRITATING AND SENSITIZING PROPENSITIES OF [redacted] ON HUMAN SKIN

1.00 **OBJECTIVES:**

.01 To identify and characterize the skin-damaging propensities that [redacted] can be induced to exercise under the conditions of this modified patch test procedure.

.02 To adjudge whether the exercise of such propensities under the test conditions contraindicates the kind of skin contact that would be occasioned during the appropriate use of the product.

2.00 **DESIGN:**

.01 A modified version of the Repeated Insult Patch Test [redacted] was conducted on a panel composed of more than one hundred subjects at the outset.

.02 The regimen comprised nine sequential 24-hour induction applications and two concurrently conducted 24-hour challenge applications, one on the initial induction site and one on a naive site.

.03 During the initial phase, the skin of the contact sites was graded and the grades recorded on Wednesdays, Fridays (i.e. twenty-four hours after patches had been removed), and Mondays (i.e. forty-eight hours after patches had been removed).

.04 During the challenge phase, the skin of the contact sites was graded within moments after the patches had been removed (24 hours post application) and again twenty-four hours later. Follow-up examinations were conducted thereafter only if adverse effects were present.

.05 This study was conducted in compliance with the standards of good clinical practices generally applicable for the protection of the privileges and well-being of individuals who participate in patch test procedures.

3.00 **SPONSOR:** [redacted]

Project Director:

Authorization:

Purchase Order:

4.00 **STUDY PRODUCT:**

Type of Product:	Face & Body Powder
Sponsor Identification:	[redacted]
Date received:	7/13/10
Quantity rec'd:	>587 g. gross wt.
Form used in study:	As supplied
PI N^{o}	[redacted]

5.00 **SITE OF STUDY:**

Product Investigations, Inc.
142 North Ninth Street
Suite 16
Modesto, CA 95350

Study Personnel:

Medical Director:	Morris V. Shelanski, MDCM
Dir. Derm. Services:	Joseph E. Nicholson III
Dermatologist:	Clinton E. Prescott Jr., MD
Technicians:	Lisa Cortez, Henry Cortez
Quality Assurance:	Samuel J. Charles III

6.00 **DATES OF STUDY:**

Started:	19 July 2010
Completed:	20 August 2010

7.00 SELECTION OF SUBJECTS:

.01 RECRUITING:

Prospective subjects were recruited from surrounding localities via phone, posters and personal contact.

.02 INFORMED CONSENT:

All individuals who expressed interest in participating were given an informed consent document to read. This document, which each candidate had to read and sign before being entered into the study, presented the following information:

a. How many subjects were to be enrolled in the study;
b. The intended use of the product;
c. Why the product was being tested;
d. How the test was to be performed;
e. That the regimen was not intended to benefit a subject's health, well being, or quality of life.
f. The different ways that participation may be detrimental to a subject's health, well being, or quality of life.
g. That not all detrimental effects could be foreseen and made known at the time the informed consent was presented for the prospective subject's signature.
h. What commitments a subject had to make to be in compliance; and
i. What considerations a subject was entitled to receive and the conditions for receiving them.

.03 DETERMINATION OF ELIGIBILITY:

Information concerning a prospective subject's qualifications was obtained from the answers the subject gave in filling out a medical history form and in responding to specific questions. Those who did not meet the following criteria were rejected.

a. **Inclusion Criteria: Satisfaction of all the following items was obligatory:**
   i. The candidate was at least eighteen years old, and
   ii. agreed to comply fully with the scheduled study regimen, and
   iii. expressed awareness that a participant would incur risks that would affect her/his well-being, and
   iv. denied that the amount of the stipend had induced her/him to participate against her/his better judgment, and
   v. had read the informed consent agreement, and
   vi. had assured the interviewer that she/he had no questions about the informed consent's contents that had not been answered to her/his satisfaction, and
   vii. had signed the consent form willingly and without reservation.

b. **Exclusion Criteria:** Any one of the following items was cause for rejection:
   i. The candidate had an illness that contraindicated participation; or
   ii. a condition that rendered the skin unsuitable for use in this study; or
   iii. was using dosages of medications that could alter the skin's tolerance; or
   iv. had a documented history of intolerance to the category of products submitted for study; or
   v. was a female who was pregnant or was breast feeding an infant.

.04 PANEL INFORMATION:

a. **Panel N°:** [redacted]

b. **Demographics:**

SEX	Number	Age Range
Female	66	18 – 76
Male	44	18 – 66

c. **Dedication:** This was a shared panel, i.e. the subjects were engaged in the evaluation of materials submitted by sponsors other than [redacted]

8.00 SITE INFORMATION:

.01 LOCATION:

[redacted] was assigned Band #1 on the right side of the back of each subject.

.02 IDENTIFICATION OF A CONTACT SITE:

At each visit the skin around the contact site was marked to facilitate examinations after the device was removed and positioning of subsequently-applied devices as precisely as was feasible on the same site.

9.00 PATCHING DEVICES:

.01 TYPE OF DEVICE:

Partially-occlusive patching devices consisting of a 2cm x 2cm absorbent pad centered on the adhesive-coated surface of a 2cm x 4cm plastic film were used to convey and maintain the product on the skin.

.02 PREPARATION OF A PATCHING DEVICE:

The webril pad of a patching device was evenly coated with 200mg of the test material.

.03 POSITIONING AND REMOVING A PATCHING DEVICE:

a. A prepared device was positioned on its designated site on each subject with the product-treated surface of the pad in contact with the skin.
b. Firm pressure was applied to the backing of the device to effect intimate contact of the pad with the skin and to bond the flanges of the device securely to the skin.
c. When the time came for removing the device, the device was peeled off the skin as gently as was feasible under the circumstances.

10.00 DATA ACQUISITION:

.01 GRADING PROCEDURE:

a. Examinations of the contact sites to grade the effects elicited by the product were conducted on Mondays, Wednesday and Fridays. When a subject came in on a scheduled examination day, the technician examined the skin of the contact site.
   i. If no adverse effect was detected, a "0" was recorded in the subject's Case Report Form.
   ii. If an adverse effect was detected, the technician entered a grade indicating her assessment of the response's intensity.
b. The subject was then sent into the patching room where the site was examined again by a second technician to ascertain independently whether or not the site should be used again. If she disagreed with the first technician's assessment, the application was held in abeyance until the issue could be resolved with the help of the supervisor and/or the investigator.
c. The supervisor or the investigator was called in not only when a disagreement had to be resolved, but also to validate substantial sudden changes, e.g. when a response is deemed to merit a grade ≥3 or when a response has been judged to have decreased by two or more points from the previous day's status.

.02 CRITERIA FOR GRADING RESPONSE INTENSITY:

The following scale was used in this procedure to designate the intensities of those gross skin changes that may be occasioned by exposing the surface of the skin to a product.

Morphology	Visible Change	Grade
Subclinical Stage	None	0
Inflammation		
Vascular Dilation:	Faint redness with poorly defined margins	1
	Redness with well-defined margins	2
Infiltration:	Redness plus well-defined edema	3
	Redness plus papules, or vesicles or ulceration	4

.04 SITE CHANGES:

a. **Switch to a Naive Site:**
   i. If the product had elicited a Grade 2 response on a subject, application of the product would have been switched immediately to a naive site on the subject.
b. **Discontinuation of Applications:**
   i. If the product had elicited a second Grade 2 on a subject, application of the product would have been discontinued immediately for the remainder of the initial phase on the affected subject.
   ii. If the product had elicited a Grade 3 response on a subject, application of the product would have been discontinued immediately for the remainder of the initial phase on the affected subject.

11.00 OVERVIEW OF STUDY REGIMEN:

	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Week #1	Apply-	Remove	Grade/Apply	Remove	Grade/Apply	(Removed)	–
Week #2	Grade/Apply	Remove	Grade/Apply	Remove	Grade/Apply	(Removed)	–
Week #3	Grade/Apply	Remove	Grade/Apply	Remove	Grade/Apply	(Removed)	–
Week #4	Grade	–	–	–	–	–	–
Week #5	Apply	Remove/Grade	Grade	Grade*	Grade*	–	–

*If necessary

12.00 STUDY REGIMEN:

.01 INITIAL/INDUCTION PHASE-

Week #1:

Monday:

i. As each subject presented herself/himself at the clinic, the skin of the contact site assigned to the product submitted for study was examined and ascertained to be suitable before applications were begun.
ii. A freshly-prepared patching device was applied on its assigned site.
iii. The skin around the device was marked and the subject was instructed to return on Tuesday.

Tuesday:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The patching device was removed by a technician and the subject was instructed to return on Wednesday

Wednesday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared patching device was applied on the same site.
iii. The site-identifying marks were reinforced and the subject was instructed to return on Thursday

Thursday:

i. As each subject returned, the site-identifying marks were reinforced.
ii. The patching device was removed by a technician and the subject was instructed to return on Friday.

Friday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. A freshly-prepared patching device was applied on the same site.
iii. The site-identifying marks were reinforced.
iv. The subject was dismissed with instructions to remove the patching device on Saturday, to record the time of removal, and to return to the clinic on the following Monday for resumption of the regimen.

Week #2:

Monday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. The time at which the patch was removed on Saturday was recorded.
iii. A freshly-prepared patching device was applied on the same site.
iv. The site-identifying marks were reinforced and the subject was instructed to return on Tuesday.

Tuesday, Wednesday, Thursday, Friday:

The procedures followed were the same as those followed on corresponding days during Week 1.

Week #3:

Monday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. The time at which the patch was removed on Saturday was recorded.
iii. A freshly-prepared patching device was applied on the same site.
iv. The site-identifying marks were reinforced and the subject was instructed to return on Tuesday.

Tuesday, Wednesday, Thursday, Friday:

The procedures followed were the same as those followed on corresponding days during Week 1.

Week #4:

Monday:

i. As each subject returned, the skin of the contact site was graded. The grade was recorded.
ii. The time at which the patch was removed on Saturday was recorded.
iii. a) If the subject had undergone all nine induction applications, she/he was dismissed after being instructed as follows:
i) to report back to the clinic on the following Monday to receive the challenge applications, and
ii) to notify the investigator without delay should any significant changes occur in the skin of the contact site before Monday of the challenge week.

b) If the subject had not received the required number of induction applications and was deficient without valid reason, applications were continued. As many as two missed applications could be made up during this week. When the subject had undergone the required number of make up applications, she/he was dismissed after being instructed as in section a) ii, above.

.02 HIATUS/MAKE UP PHASE-
Week # 4:

After the examination on Monday of Week 4, no procedures other than make-up cycles were scheduled during this period.

.03 CHALLENGE PHASE-
Week #5:

Monday:

i. As each subject returned, the skin of the initial induction site was examined and ascertained to be free of any conditions that would have rendered it unfit for undergoing the challenge applications.
ii. A prepared device was applied on the initial induction site.
iii. A second prepared device was applied on a naive site.
iv. The skin around both devices was marked and the subject was instructed to return on Tuesday.

Tuesday: (Note: If a subject was absent on Monday, she/he was patched on Tuesday.)

i. As each subject returned, the site-identifying marks around both contact sites were reinforced.
ii. Both patching devices were removed by a technician.
iii. The skin of both contact sites was graded; the grades were recorded.
iv. The subject was instructed to return on Wednesday.

Wednesday:

i. As each subject returned, the skin of both contact sites was graded; the grades were recorded.
ii. If follow-up was indicated, the subject was instructed to return on Thursday, otherwise the subject was dismissed from the study of this material.

.04 FOLLOW-UP PHASE:

Week No. 6 and Week No. 7:

During the two weeks following the exit examination, the subjects were given the opportunity to relay any information concerning effects that were relevant to the characterization of the product as well as to communicate the need for treatment of persistent or newly-occurring responses.

13.00 PROCEDURE DEVIATIONS:

No deviations in procedure were necessary.

14.00 COMPLIANCE

	No. Of AEC's		COMPLIANT	
PHASE	Required	EXCUSED	YES	NO
Induction	8	0	106	4
Challenge	1/1	0	105	5

106 of the 110 Subjects were in compliance with the number of required application/examination cycles during induction.
105 of the 110 Subjects were in compliance with the number of required application/examination cycles during challenge.

15.00 INCIDENCE OF RESPONSES:

Grade	Type of Response	Induction Phase	Challenge Phase	
			Original Contact Site	Naive Contact Site
0	No visible change	108 subjects	105 subjects	105 subjects
1	Faint redness, undefined border	0 "	0 "	0 "
2	Intense redness, defined border	0 "	0 "	0 "
3	Redness + definite edema	0 "	0 "	0 "
4	Redness + papules, or vesicles, etc.	0 "	0 "	0 "
	No. of Responders	0 subjects	0 subjects	0 subjects
	No Data Acquired	2 subjects	5 subjects	5 subjects

16.00 SIGNIFICANCE OF THE RESPONSES:

.01 Initial/Induction Phase:

No responses were noted on any of the 108 subjects who underwent at least one post-application examination. The absence of responses characterizes the product as one which is devoid of clinically significant skin-irritating propensities.

.02 Challenge Phase:

a. **Original Contact Sites:**
No responses were noted on any of the 105 subjects who participated in this phase of the study. The absence of responses characterizes the product as one which is devoid of clinically significant skin sensitizing propensities.

b. **Naive Contact Sites:**
No responses were noted on any of the 105 subjects who participated in this phase of the study. The absence of responses characterizes the product as one which is devoid of clinically significant skin sensitizing propensities.

17.00 CONCLUSIONS:

.01 [redacted] was found to be neither a clinically significant skin irritant nor a skin sensitizer under the conditions of this study.

.02 [redacted] is not contraindicated for usages entailing repeated applications on human skin under conditions appropriate for such products.

PRODUCT INVESTIGATIONS, INC.

9/2/10
Date

Joseph E. Nicholson III
Director, Dermatological Studies

18.00 COMPLIANCE WITH GOOD QUALITY ASSURANCE STANDARDS:

I have audited the results presented in this report and believe that, to the best of my knowledge, they accurately reflect the raw data acquired during the course of this study.

Samuel Charles
Director, Quality Assurance

[redacted]

Site: R1

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 5					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	
1	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
2	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
3	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
4	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
5	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
6	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
7	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
8	B	[redacted]	A	[redacted]	Dropped		[redacted]		[redacted]			[redacted]		[redacted]												
9	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
10	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
11	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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13	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
14	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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16	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
17	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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21	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
22	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
23	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
24	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
25	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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30	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			

A = Absent

(Grade) / (Grade) = Original Site / Naive Site

[redacted]

Site: R1

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 5					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	
31	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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33	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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43	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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46	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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49	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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52	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
53	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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55	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
56	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
57	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
58	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
59	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
60	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			

A = Absent

(Grade) / (Grade) = Original Site / Naive Site

[redacted]

Site: R1

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 5					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	
61	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
62	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
63	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
64	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
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66	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
67	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
68	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
69	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
70	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
71	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
72	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
73	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
74	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	Dropped		[redacted]		[redacted]												
75	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
76	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
77	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
78	B	[redacted]	0	[redacted]	Dropped		[redacted]		[redacted]			[redacted]		[redacted]												
79	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
80	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
81	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
82	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
83	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
84	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					A	B	0/0			
85	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
86	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
87	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
88	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
89	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			
90	B	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0	[redacted]	0	[redacted]	0	0					B	0/0	0/0			

A = Absent

(Grade) / (Grade) = Original Site / Naive Site

[redacted]

Site: R1

Subj #	INDUCTION PHASE															HIATUS/MAKEUPS					CHALLENGE PHASE					
	WEEK 1					WEEK 2					WEEK 3					WEEK 4					WEEK 5					
	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	M	T	W	TH	F	
91	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
92	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
93	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
94	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
95	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
96	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
97	B		0		0	0		0		0	0		0		0	0					A	B	0/0			
98	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
99	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
100	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
101	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
102	B		0		0	0		0		0	0		A		0	0					Dropped					
103	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
104	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
105	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
106	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
107	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
108	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
109	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			
110	B		0		0	0		0		0	0		0		0	0					B	0/0	0/0			

A = Absent

(Grade) / (Grade) = Original Site / Nalve Site

Personal Care Products Council
Committed to Safety, Quality & Innovation

Memorandum

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

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

DATE: July 8, 2019

SUBJECT: Triticum Vulgare (Wheat) Bran Extract

Anonymous. 2019. Summary Information - Triticum Vulgare (Wheat) Bran Extract.

1620 L Street, N.W., Suite 1200 | Washington, D.C. 20036 | 202.331.1770 | 202.331.1969 (fax) | www.personalcarecouncil.org

July 2019

Summary Information – Triticum Vulgare (Wheat) Bran Extract

The extracts described below are all derived from food-grade plant material.

The process for all four extracts: The plant material is extracted at considerate temperatures during a fixed time and sterile filtered at the end of the fabrication

	Glycerin Extract	Propylene Glycol Extract	Propylene Glycol Extract	Soybean Oil Extract
INCI names and Composition	Glycerin 75-100% Water 10-25% Triticum Vulgare (Wheat) Bran Extract 5-10%	Propylene Glycol 75-100% Triticum Vulgare (Wheat) Bran Extract 10-25%	Propylene Glycol 95-100% Triticum Vulgare (Wheat) Bran Extract 1-5%	Glycine Soja (Soybean) Oil 75-100% Triticum Vulgare (Wheat) Bran Extract 10-25%
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 (pH regulation)	None	0.1-1% Lactic Acid (pH regulation)	<0.1% DL-alpha-Tocopherol (stabilizer)
Aspect	Clear, yellow-brown colored liquid	Clear, yellow-brown colored liquid	Clear, yellowish colored liquid	Clear, yellowish colored liquid
Odor	Faint herbal odor	Typical odor	Faint odor	Faint odor
pH-value	4.0-5.0	4.0-5.0	4.5-5.5	-
Proof of identity	HPLC	HPLC	HPLC	-
Bacteriological control	Max. 100 germs/ml	Max. 100 germs/ml	Max. 100 germs/ml	Max. 100 germs/ml
Refraction index	1.440-1.470 (20°C)	1.425-1.445 (20°C)	1.425-1.445 (20°C)	1.460-1.480
Density	1.200-1.240 (20°C)	1.035-1.055 (20°C)	1.035-1.055 (20°C)	0.910-0.930
Color number (Lovibond)	3-7	6-10	1-3	1-3
Heavy metals (solvent)	Total heavy metals (as PB) ≤5 ppm	Not tested	Not tested	Not tested

Personal Care Products Council
Committed to Safety, Quality & Innovation

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 22, 2019

SUBJECT: Scientific Literature Review: Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics (release date June 19, 2019)

The Personal Care Products Council (PCPC) has no suppliers listed for:

Triticum Turgidum Durum (Wheat) Seed Extract
Triticum Vulgare (Wheat) Flour Extract
Triticum Vulgare (Wheat) Germ Powder
Triticum Vulgare (Wheat) Bran Lipids

The Council respectfully submits the following comments on the scientific literature review, Safety Assessment of Wheat-Derived Ingredients as Used in Cosmetics.

Key Issue

It is not clear that ECHA has been searched for wheat-derived ingredients. A dossier on Wheat, ext. has been submitted to ECHA that includes a genotoxicity assay on a wheat germ glyceride, and may include additional useful information.

Additional Considerations

Introduction - In addition to citing a 1980 CIR report for the statement that gluten in cosmetics should not be problem, perhaps the following more recent reference may also be helpful (this reference does not have an abstract):

Thompson T, Grace T. 2012. Gluten in cosmetics: is there a reason for concern? *J Acad Nutr Diet* 112(9): 1316-1323.

Definition and Plant Identification - This section should mention that *Triticum vulgare* is a synonym of *Triticum aestivum*. In addition to citing the Dictionary, a reference such as the Agricultural Research Services GRIN database (https://npgsweb.ars-grin.gov/gringlobal/taxon/taxonomysimple.aspx) should be cited.

Non-Cosmetic Use, food - Without the listing of the sources considered major allergens by the FDA, the following sentence does not make sense: "A major food allergen is an

ingredient from a food or food group, such as wheat, that contains protein derived from the food."

It would be helpful to indicate that wheat gluten is considered to be GRAS for food (21CFR184.1322).

Non-Cosmetic Use, drugs; Summary - According to reference 36, "bran", not specifically, "wheat bran" is listed as a laxative. It is not correct to state that wheat germ is an OTC weight control product as 21CFR310-545 is the part of the *Federal Register* that lists actives with inadequate evidence to support safety and effectiveness. Reference 36 also lists wheat germ for weight control products as being in category II: "not generally recognized as safe and effective or unacceptable indications".

Toxicological Studies; Summary - It is not appropriate to imply that oral exposure to wheat has the potential to cause systemic effects.

Reproductive and Developmental Toxicity - The CIR report outline at https://www.cir-safety.org/sites/default/files/CIR%20Report%20Format%20Outline.pdf calls this section "DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES".

DART; Summary; Reference 40 - Benzo[α]pyrene needs to be corrected to benzo[a]pyrene.

DART - What was the dose for the mice that received only wheat sprout extract?

Anti-Mutagenicity - Please describe the "S-30 fraction".

Tumor Promotion; Anti-Tumor Promotion - It is not clear why reference 40 and reference 43 are presented in different subsections as both studies show a lack of tumor promotion activity for the wheat-derived ingredient that was tested.

Irritation and Sensitization - As the HRIPT on a powder containing 13% Triticum Vulgare (Wheat) Germ Extract was provided by industry, the statement "and unpublished data were not submitted", needs to be deleted.

Table 2 - It is not clear why all the plant parts are included in Table 2 as some, such as root, are not sources of the wheat ingredients under review in this report.

Reference 41 - The title of this reference suggests that a 90-day study of a wheat bran extract was completed in rats. It is not clear why this study was not included in the CIR report.