Safety Assessment of Yeast-Derived Ingredients as Used in Cosmetics

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*All interested persons are provided 60 days from the above release date (i.e., **March 10, 2024**) to comment on this safety assessment, and to identify additional published data that should be included or provide unpublished data which can be made public and included. Information may be submitted without identifying the source or the trade name of the cosmetic product containing the ingredient. All unpublished data submitted to the Cosmetic Ingredient Review (CIR) will be discussed in open meetings, will be available for review by any interested party, and may be cited in a peer-reviewed scientific journal. Please submit data, comments, or requests to the CIR Executive Director, Dr. Bart Heldreth.*

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ABBREVIATIONS

2-AA	2-aminoanthracene
2-NF	2-nitrofluorene
9-AA	9-aminoacridine
ADME	absorption, distribution, metabolism, and excretion
AF-2	2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide
ALT	alanine aminotransferase
AOP	adverse outcome pathway
ARE	antioxidant response element
BAL	bronchoalveolar lavage
BSL	biosafety level
B16F10	melanocytes
Caco-2	human colon epithelial cells from a male with colorectal adenocarcinoma
CAS	Chemical Abstracts Service
CFR	Code of Federal Regulations
CFU	colony-forming units
CIR	Cosmetic Ingredient Review
CL	chemiluminescence
Council	Personal Care Products Council
DART	Developmental and Reproductive Toxicity
Dictionary	web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI)
DLD1	human colorectal adenocarcinoma cell line
DNA	deoxyribonucleic acid
dpm	disintegrations per minute
DPRA	direct peptide reactivity assay
ECHA	European Chemicals Agency
EFSA	European Food Safety Authority
ENNG	1-ethyl-2-nitro-3-nitroguanidine
EP-2	natural yeast extract isolated by ethanol precipitation
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
GPMT	guinea pig maximization test
GRAS	generally recognized as safe
GST	glutathione S-transferase
HaCaT	human keratinocytes
HCC70	non-metastatic breast cancer cell line
HCT116	human colorectal carcinoma cell line
h-CLAT	human cell line activation test
HeLa	human cervical cancer cells
HRIPT	human repeated-insult patch test
HSCAS	hydrated sodium calcium aluminosilicate
ICU	intensive care unit
IFN	interferon
IgA	immunoglobulin A
IgE	immunoglobulin E
IgG	immunoglobulin G
IL	interleukin
kDa	kilodaltons
KE	key event
LC-MS/MS	liquid chromatography-tandem mass spectrometry
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LDH	lactate dehydrogenase
LLNA	local lymph node assay
MCF-7	human breast cancer line with estrogen, progesterone, and glucocorticoid receptors
α-MSH	α-melanocyte-stimulating hormone
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide
NCBI	National Center for Biotechnology Information
NOAEL	no-observed-adverse-effect-level
NR	not reported
Nrf2	nuclear factor erythroid 2-related factor 2
OECD	Organisation for Economic Cooperation and Development

OPPTS	Office of Prevention, Pesticides, and Toxic Substances
Panel	Expert Panel for Cosmetic Ingredient Safety
PBS	phosphate-buffered saline
PEFR	peak expiratory flow rate
PMN	polymorphonuclear leukocytes
QPS	qualified presumption of safety
RAST	radioallergosorbent test
SI	stimulation index
S180	murine sarcoma cancer cell line
SCC-4	squamous cell carcinoma of the tongue
SPF	specific pathogen-free
TG	test guidelines
TGF	transforming growth factor
T_{max}	time to maximum blood concentration
t_{50}	duration of exposure resulting in a 50% decrease in MTT conversion
THP-1	human monocytic cell line
US	United States
U-SENS™	U937 cell line activation test
UVA	ultraviolet A
VCRP	Voluntary Cosmetic Registration Program
ZR-75-1	mammary gland epithelial cell line from a female with ductal carcinoma

ABSTRACT

The Expert Panel for Cosmetic Ingredient Safety (Panel) assessed the safety of 56 yeast-derived ingredients. These ingredients are mostly reported to function in cosmetics as skin protectants or skin-conditioning agents. Industry should continue to use good manufacturing practices to minimize impurities that could be present in yeast-derived ingredients, such as heavy metals and pesticide residues, according to limits set by the US Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA). The Panel reviewed the available data to determine the safety of these ingredients and concluded that 11 yeast-derived ingredients and 22 generic-named yeast-derived ingredients, when derived from species of yeast included in the report with both dermal sensitization and food use status, are safe in cosmetics in the present practices of use and concentration described in this safety assessment. The Panel also concluded that the available data are insufficient to make a determination of safety for the remaining 23 ingredients under the intended conditions of use in cosmetic formulations.

INTRODUCTION

This assessment reviews the safety of the following 56 yeast-derived ingredients as used in cosmetic formulations:

Galactomyces Ferment Filtrate
Hydrolyzed Candida Bombicola Extract
Hydrolyzed Candida Saitoana Extract
Hydrolyzed Kluyveromyces Extract
Hydrolyzed Metschnikowia Agaves Extract
Hydrolyzed Metschnikowia Reukaufii Extract
Hydrolyzed Metschnikowia Shanxiensis Extract
Hydrolyzed Saccharomyces Cell Wall
Hydrolyzed Saccharomyces Extract
Hydrolyzed Saccharomyces Lysate Extract
Hydrolyzed Torulaspora Delbruekii Extract
Hydrolyzed Yeast
Hydrolyzed Yeast Extract
Kluyveromyces Extract
Lactic Yeasts
Lipomyces Lipid Bodies
Lipomyces Oil
Lipomyces Oil Extract
Metschnikowia Agaves Extract
Metschnikowia Henanensis Extract
Metschnikowia Reukaufii Lysate Extract
Metschnikowia viticola Extract
Pichia Anomala Extract
Pichia Caribbica Ferment
Pichia Extract
Pichia Ferment Extract Filtrate
Pichia Ferment Lysate Filtrate
Pichia Heedii Extract
Pichia Minuta Extract
Pichia Pastoris Ferment Filtrate
Phaffia Rhodozyma Extract
Phaffia Rhodozyma Ferment Extract
Saccharomyces
Saccharomyces Cerevisiae Extract
Saccharomyces Extract
Saccharomyces Ferment
Saccharomyces Ferment Extract
Saccharomyces Ferment Extract Lysate Filtrate
Saccharomyces Ferment Filtrate
Saccharomyces Ferment Lysate Extract
Saccharomyces Ferment Lysate Filtrate
Saccharomyces Lysate
Saccharomyces Lysate Extract
Saccharomyces Lysate Extract Filtrate
Saccharomyces Lysate Filtrate
Schizosaccharomyces Ferment Extract Filtrate
Schizosaccharomyces Ferment Filtrate
Schizosaccharomyces Pombe Extract
Torulaspora Delbrueckii Extract
Torulaspora Delbrueckii Ferment
Yarrowia Lipolytica Extract
Yarrowia Lipolytica Ferment Lysate
Yarrowia Lipolytica Oil
Yeast
Yeast Extract
Yeast Ferment Extract

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook* (wINCI; *Dictionary*), the majority of these ingredients are reported to function in cosmetics as skin protectants or skin-conditioning agents (Table 1).[1] Other reported functions for this ingredient group include hair-conditioning agent, surfactant, humectant, antioxidant, colorant, anti-acne agent, anti-microbial agent, film former, and viscosity-increasing agent.

Some of the species of yeast reviewed in this report are naturally present or are used in foods (e.g., *Saccharomyces cerevisiae* is generally recognized as safe (GRAS) as a flavoring agent and adjuvant at a level not to exceed 5% in food [21CFR184.1983]). For the ingredients that are affirmed GRAS or are used/present in foods, systemic toxicity via the oral route will not be the focus of this safety assessment. Although oral exposure data are included in this report, the primary focus for the safety of such ingredients is topical exposure and local effects.

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 extensive search of the world's literature; a search was last conducted October 2023. A listing of the search engines and websites that are used and the sources that are typically explored, as well as the endpoints that the Panel typically evaluates, is provided on the Cosmetic Ingredient Review (CIR) website (https://www.cir-safety.org/supplementaldoc/preliminary-search-engines-and-websites; https://www.cir-

safety.org/supplementaldoc/cir-report-format-outline). Unpublished data are provided by the cosmetics industry, as well as by other interested parties.

Some of the data included in this safety assessment were found on the European Chemicals Agency (ECHA) website.[2] Please note that the ECHA website provides summaries of information generated by industry, and it is those summary data that are reported in this safety assessment when ECHA is cited**.**

The cosmetic ingredient names, according to the *Dictionary*, are written as listed above, without italics and by capitalizing the first letter of each word in the name. In many of the published studies, it is not known how the substance being tested compares to the ingredient as used in cosmetics. Therefore, if it is not known whether the ingredient being discussed is a cosmetic ingredient, for the generic yeast ingredients, the name of the test substance will be written using all lower-case letters (e.g., yeast extract); however, if it is known that the substance is a cosmetic ingredient, the first letter of each word in the name will be capitalized (e.g., Yeast Extract). For the genus/species ingredients, if it is not known whether the ingredient being discussed is a cosmetic ingredient, the standard scientific practice of using italics will be followed (e.g., *Saccharomyces cerevisiae* extract); if it is known that the substance is a cosmetic ingredient, the *Dictionary* terminology (e.g., Saccharomyces Cerevisiae Extract) will be used.

In many instances, data were found on the species of yeast (e.g., *Yarrowia lipolytica*), and not on specific ingredients that are reviewed in this report (e.g., Yarrowia Lipolytica Ferment Lysate). Because of this, information is primarily organized by species names, rather than ingredient names, throughout the report. However, when it is known that the test substance used is a cosmetic ingredient, the INCI name will be used. It should be noted that some ingredients reviewed in this report (e.g., Galactomyces Ferment Filtrate) may be derived from more than one species of yeast (i.e., Galactomyces Ferment Filtrate may be derived from *Galactomyces candidus*, *Galactomyces fermentans*, or *Galactomyces reessii*).

In addition, many of the species of yeast reviewed in this report have synonymous names, according to the National Center for Biotechnology Information (NCBI) taxonomy database. When studies state the use of a yeast species (e.g., *Starmerella bombicola*) that is synonymous to a species reviewed in this report (e.g., *Candida bombicola*), the species name stated in the study is used as the header (e.g., *Starmerella bombicola*), with a notation stating the synonymous species that is relevant to this report (e.g., *Starmerella bombicola* (synonymous to *Candida bombicola*)).

It should also be noted that the generic yeast ingredients (e.g., Yeast Extract) named in this report may refer to several different species of yeast under the class Saccharomycetes. (Species known to be used in the formulation of Yeast Extract are listed in the Composition section of this report.) When the species of a generic ingredient is known (e.g., *Candida saitoana*), and the ingredient is a known cosmetic ingredient, it will be stated in text (e.g., Yeast Extract derived from *Candida saitoana*), and data will be associated with the specific ingredients derived from the species. Data on any species that is reported to be used in generic yeast ingredients, and is not known to be a cosmetic ingredient, will be named in the report as the species name (e.g., *Candida oleophila*). In addition, because the *Dictionary* does not define the species of yeast used in the production of these generic ingredients, when data are provided on these ingredients, the generic ingredient name will be used as the header, instead of a species name.

CHEMISTRY

Definition

According to the *Dictionary*, Yeast (CAS No. 68876-77-7) is a class of microorganisms (Saccharomycetes) characterized by a lack of photosynthetic ability, existence as unicellular or simple irregular filaments, and reproduction by budding or direct division.[1] *Saccharomyces cerevisiae,* a yeast strain widely used in the preparation of foods and cosmetics, is a highly adaptable, unicellular fungus, capable of growth both aerobic and anaerobically.[3-5] All ingredients reviewed in this report are derived from various yeast species. The definitions of the ingredients included in this report are provided in Table 1.

Yeasts are ubiquitous microorganisms that may be present in a diverse range of habitats, including the air, animals, water, and plants.[6,7] Yeasts are typically nomadic, resilient, and are able to survive in a wide range of conditions. In addition, phenotypic characteristics of yeasts may vary dependent upon environment.[8] Although yeasts can be found in natural habitats, they are typically laboratory-grown for industrial purposes.

Chemical Properties

Dried yeast (derived from *Saccharomyces cerevisiae*) occurs in the form of powder, granules, or flakes, and is typically light brown to buff in color.[9] According to a supplier, a Saccharomyces Cerevisiae Extract was reported to be a clear, yellow-colored liquid, with a pH value of 4.0 - 5.0, and a density of 1.035 - 1.055 (at 20° C).[10] The water solubility of a *Saccharomyces cerevisiae* extract is reported to be > 200 g/l, with the majority of particle sizes ranging from 50 to 220 µm (only 3% of particles < 10 µm in size).[2] Other properties of yeast-derived ingredients can be found in Table 2.

Taxonomy

The majority of the ingredients in this report, including the generic yeast ingredients (e.g., Yeast Extract), correspond to yeasts that are part of the Saccharomycetes class.[1] However, ingredients derived from the species *Phaffia rhodozyma* and the

genus *Schizosaccharomyces* belong to the class Tremellomycetes and Schizosaccharomycetes, respectively.[11] The taxonomic profile, as well as relevant synonymous genus/species names of these ingredients, are provided in Table 3.

Yeast Strain Identification and Biosafety

In order to ensure the proper strain of yeast is used in manufacturing, taxonomic identification is performed, typically via r-28S deoxyribonucleic acid (DNA) sequencing and Internal Transcribed Space.[12] According to the US Centers for Disease Control and Prevention, biosafety level (BSL) classifications are given to biological agents, including yeasts, based on the level of protection provided to workers, the environment, and the public. These levels range from 1 (no or low individual and community risk; e.g., baker's yeast) to 4 (high individual and community risk; e.g., Ebola virus). According to a manufacturer, only BSL-1 yeast species should be used in the manufacture of cosmetic ingredients. In Europe and the US, pathogenic yeasts under the Saccharomycetes class with a BSL-2 categorization include *Candida auris*, *Candida albicans*, *Candida dubliniensis*, *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis*, none of which are used in the manufacturing of cosmetic ingredients.

Method of Manufacture

Unpublished data were submitted describing methods of manufacture for some of these ingredients. Additionally, general methods of manufacture were found in the published literature; it is unknown if the general methodologies described herein apply to the manufacture of cosmetic ingredients.

According to a manufacturer, yeast ingredients are manufactured via atomization, high temperature enzymatic inactivation (80°C), addition of preservatives, freezing, mechanical grinding, ultrafiltration (0.45 µm or sterilizing filtration (0.22 µm), autolysis/lysis, and acid pH adjustment.[12] Because yeasts are only viable at temperatures < 50°C, no live yeasts would be present in the finished cosmetic product.

Hydrolyzed Saccharomyces Cell Wall

According to a manufacturer, Hydrolyzed Saccharomyces Cell Wall is prepared via the enzyme treatment, acid treatment, and neutralization of *Saccharomyces pastorianus*.[13] Supernatants are removed to produce the final product.

Kluyveromyces marxianus (synonymous to *Kluyveromyces fragilis*) and *Saccharomyces cerevisiae*

Extract powders (derived from *Kluyveromyces marxianus* and *Saccharomyces cerevisiae*) are created by first producing yeast biomass via molasses (medium of cultivation).[14] Molasses solutions (molasses and distilled water) are subjected to heavy metal removal, boiled, autoclaved, cooled, filtered, and fermented. Yeast cultures are inoculated into the bioreactor and subjected to a fermentation process under aerobic conditions. After fermentation, the fermentation medium is centrifuged, and the supernatant is decanted and the pellet is washed with saline and centrifuged again. Yeast cells are autolyzed, cooled, and centrifuged to remove cell wall components. The supernatant is then dried in a freeze-dryer, yielding the extract powder.

Lipomyces starkeyi

Lipomyces starkeyi oil is prepared by first culturing the yeast, followed by cell crushing, filtration, organic solvent extraction, and oil purification.[15] The cell crushing process is performed using a high-pressure homogenizer, and performed until particle sizes are less than 3 µm. Examples of organic solvents used for extraction include hexane, ethanol, and 2-propanol.

Saccharomyces cerevisiae

In order to obtain a baker's yeast extract (derived from *Saccharomyces cerevisiae*), dry baker's yeast (50 g) is ground using a mortar, and stirred overnight with water (100 ml).[16] The mixture is then centrifuged for 30 min, filtered, dialyzed, and freeze-dried, ultimately obtaining approximately 1 g baker's yeast extract.

Saccharomyces Cerevisiae Extract

According to data submitted by industry, Saccharomyces Cerevisiae Extract is prepared via an extraction using 1,2-propylene glycol.[10] The extract is sterile filtered and combined with 0.35% potassium sorbate and 0.35% sodium benzoate for preservation. According to a different industry submission, Saccharomyces Cerevisiae Extract is prepared by first concentrating or spray-drying a solution obtained via yeast autodigestion.[17] The resulting solution is extracted with purified water, filtered, and evaporated. The remaining substance is then combined with either ethanol or 1,3-butylene glycol, followed by sedimentation, filtration, and combination with 50% ethanol or a 50% butylene glycol solution.

Yarrowia lipolytica

A biomass of *Yarrowia lipolytica* is prepared by first grafting the yeast from an agar slant.[18] Proliferation of the yeast is continued in tanks of increasing capacity with consistent culture conditions. Yeast is harvested (centrifuged, rinsed with water, and again centrifuged) after the appropriate concentration of yeast dry matter is reached, followed by drying until a moisture content of < 5% is reached (yeast are killed during this step).

Yeast Extract

According to a manufacturer, Yeast Extract is prepared via extraction with a specified eluent (e.g., water, butylene glycol, glycerin, propylene glycol, carthamus tinctorius (safflower) seed oil), to yield a concentrate.[19] The concentrate is then blended with a diluent and preservation system to produce the final result. According to a different manufacturer, Yeast Extract is prepared via solubilization of yeast (e.g., *Candida saitoana*) in water, separation of soluble and insoluble phases, filtration, followed by sterile filtration.[20]

Composition and Impurities

Candida kefyr (synonymous to *Kluyveromyces fragilis*)

The total saturated, monounsaturated, and polyunsaturated fatty acid composition of *Candida kefyr* was determined to be 23.79, 52.79, and 23.42% (of total fatty acids), respectively (measured via gas chromatography mass spectrometry).[21] The specific fatty acids observed can be found in Table 4.

Hydrolyzed Saccharomyces Cell Wall

According to a manufacturer, Hydrolyzed Saccharomyces Cell Wall may be derived from the yeast species *Saccharomyces bayanus*, *Saccharomyces cerevisiae*, or *Saccharomyces pastorianus*.[13] This ingredient should not contain more than 2 µg/g lead, 1.5 µg/g arsenic, and 5.6% nitrogen.

Kluyveromyces fragilis

The composition of a biomass of *Kluyveromyces fragilis* grown on deproteinized whey supplemented with 0.8% diammonium hydrogen phosphate and 10 ppm indole-3 acetic acid was evaluated.[22] The biomass was reported to consist of 37 g/100 g crude protein, 16 g/100 g ash, 4.9 g/100 g crude fiber, 7.8 g/100 g fat, and 34.3 g/100 g carbohydrates. Also reported was a total nitrogen content of 5.92% and total nucleic acid content of 4.82% in *Kluyveromyces fragilis* cells. The essential amino acid profile of the biomass is as follows: arginine (4.30 g/100 g protein), histidine (1.98 g/100 g protein), isoleucine (3.82 g/100 g protein), leucine (5.47 g/100 g protein), lysine (6.91 g/100 g protein), methionine (0.38 g/100 g protein), phenylalanine (3.98 g/100 g protein), threonine (4.45 g/100 g protein), tryptophan (1.07 g/100 g protein), and valine (5.02 g/100 g protein).

Kluyveromyces lactis

A quantitative analysis of sterols in *Kluyveromyces lactis* cells was performed using high-performance liquid chromatography.[23] Ergosterol represented more than 80% of the total amount of yeast sterols.

Kluyveromyces marxianus

Prominent volatile compounds found in a *Kluyveromyces marxianus* extract include hexadecane, pentanoic acid, phenol, γ-decalactone, 3-octanone, and 2-methylpentanal.[14] Other volatile compounds found in this extract in lesser amounts include acetic acid, 2-phenylethyl ester, benzaldehyde, 2,3-butanediol, 2-ethyl,3,5-dimethylpyrazine, nonanal, benzyl alcohol, 2-phenylethanol, (-)-citronellol, geranyl acetate, 2,3,5-trimethylpyrazine, pentadecane, 2-phenyl-2-butenal, tetradecane, 2-nonanone, ethyl phenylacetate, β-myrcene, 2-ethyl-2,5-dimethylpyrazine, and 2-ethyl-6-methylpyrazine. This extract was reported to contain amino acids in an amount of 42.31 g/100 g protein). Alpha-mannans are reported to be present in *Kluyveromyces marxianus* cell walls.[24]

Lipomyces Lipid Bodies

Full genomic sequencing and polymerase chain reaction tests were performed on a cream containing 100% Lipomyces Lipid Bodies.[25] This cream contained no foreign genes or antibiotic resistance traits.

Lipomyces starkeyi

The main component of *Lipomyces starkeyi* is triacylglycerides.[15] Yeast oil derived from this species is rich in palmitic and oleic acid.

Phaffia rhodozyma

The sterol, ubiquinone, and carotenoid content of a *Phaffia rhodozyma* yeast biomass sample consisted of the following: ergosterol 1.121 ± 0.013 mg/g, ubiquinone 1.548 ± 0.009 mg/g, torularhodin 0.856 ± 0.009 mg/g, torulene 0.058 ± 0.002 mg/g, and beta-carotene 0.024 ± 0.001 mg/g.[26] This biomass sample contained 20% saturated fatty acids, 42% monounsaturated fatty acids, and 38% saturated fatty acids.

Saccharomyces cerevisiae

In order for baker's yeast extract (mechanically ruptured cells of *Saccharomyces cerevisiae*) to meet GRAS specifications for food use, the ingredient must contain, on a dry weight basis, < 0.4 ppm arsenic, < 0.13 ppm cadmium, < 0.2 ppm lead, < 0.05 ppm mercury, < 0.09 ppm selenium, and < 10 ppm zinc [21CFR184.1983]. In addition, dried yeast (*Saccharomyces cerevisiae*) may be safely used in food provided the total folic acid content of the yeast does not exceed 0.04 mg/g yeast [21CFR172.896]. The composition of a cleaned natural yeast (*Saccharomyces cerevisiae*; g/100 g dry yeast) was reported to be 42.83 ± 0.11 protein, 1.45 ± 0.40 total lipids, 1.74 ± 0.17 ashes, and 53.91 carbohydrates.[27] This sample of yeast contained moisture in an amount of approximately 0.07 g/100 g dry yeast.

The essential amino acid profile, amount of mineral elements, and fatty acid composition of whole yeast cells (*Saccharomyces cerevisiae*) was evaluated.[28] The mineral elements observed in the largest quantities were phosphorous (1516.0 mg/100 g) and potassium (2035 mg/100 g). All other mineral elements were present in amounts of 147.7 mg/100 g or less. The essential amino acids observed were threonine (4.7 g/100 g protein), methionine + half-cystine (2.4 g/100 g protein), valine (4.8 g/100 g protein), isoleucine (4.2 g/100 g protein), leucine (6.0 g/100 g protein), tyrosine + phenylalanine (6.5 g/100 g protein), lysine (8.0 g/100 g protein), histidine (4.2 g/100 g protein), and tryptophan (1.2 g/100 g protein). The total saturated and monounsaturated fatty acid composition in *Saccharomyces cerevisiae* was determined to be 29.32 and 70.69% (of total fatty acids), respectively (measured via gas chromatography mass spectrometry). The specific fatty acids observed can be found in Table 4. In addition, the nutrient, amino acid, and mineral composition of a *Saccharomyces cerevisiae* sample can be found in Table 5.

The main classes of lipids observed in *Saccharomyces cerevisiae* extracts were determined to be glycerophospholipids, sphingolipids, sterols, and glycerolipids.[29] Forty percent of the identified lipids were polar lipids, while the remaining 60% were neutral lipids. In addition, the cell wall of *Saccharomyces cerevisiae* contains layers predominantly consisting of beta-glucans.[30] The inner layer of the cell wall contains (1→3) β- and (1→6) β-linked glucose residues, and chitin. The outer layer of the cell wall is mainly composed of α-mannan and glycoproteins.

Prominent volatile compounds found in a *Saccharomyces cerevisiae* extract include acetic acid, 2-phenylethyl ester, benzaldehyde, 2,3-butanediol, 2-ethyl-3,5-dimethylpyrazine, nonanal, benzyl alcohol, 2-phenylethanol, (-)-citronellol, hexadecane, and pentanoic acid.[14] Other volatile compounds found in lesser amounts include phenol, γ-decalactone, 3-octanone, 2-methylpentanal, geranyl acetate, 2,3,5-trimethylpyrazine, pentadecane, 2-phenyl-2-butenal, tetradecane, 2-nonanone, ethyl phenylacetate, β-myrcene, 3-ethyl-2,5-dimethylpyrazine, and 2-ethyl-6-methylpyrazine. This extract was reported to be rich in amino acids (47.41 g/100 g protein).

The chemical composition of yeast hydrolysate obtained from *Saccharomyces cerevisiae* was reported to be 4.7% moisture, 68.3% crude protein, 0.3% crude lipid, 3.1% crude ash, and 23.6% carbohydrate.[31]

According to the Food Chemicals Codex, dried yeast (*Saccharomyces cerevisiae*) may not contain more than 1 mg/kg lead.[9] In addition, dried yeast may not contain more than 8% ash.

Saccharomyces Cerevisiae Extract

According to a supplier, Saccharomyces Cerevisiae Extract may not contain more than 20 ppm heavy metals or 2 ppm arsenic.[17]

Schizosaccharomyces pombe

The fatty acid profile of a *Schizosaccharomyces pombe* extract was evaluated via gas chromatography.[32] These fatty acids include palmitic acid (C16:0), palmitoleic acid (C16:1), stearic acid (C18:0), and oleic acid (C18:1). The *Schizosaccharomyces pombe* cell wall contains two electron-dense layers formed by galactomannan and a central electron-transparent layer consisting of β- and α-glucans (e.g., β-(1,3)-, β-(1,6)-, and α-(1,3)-glucan).[33]

Yarrowia lipolytica

Yeast biomass derived from *Yarrowia lipolytica* (a novel food according to the European Food Safety Authority (EFSA)) is reported to consist primarily of proteins (45 - 55 g/100 g), dietary fiber (25 g/100 g), and fat (7 - 10 g/100 g (the majority being mono-and polyunsaturated fatty acids).[18] When pesticide evaluations were performed on yeast biomass samples, the analyzed pesticides (e.g., organochlorinated and organophosphate pesticides, pyrethroids) were below limits of quantification. Specifications for yeast biomass derived from *Yarrowia lipolytica* as a novel food include the following: ≤ 3.0 mg/kg lead, ≤ 1.0 mg/kg cadmium, ≤ 0.1 mg/kg, ≤ 5000 colony-forming units (CFU)/g total aerobic microbial count, ≤ 100 CFU/g total yeast and mold count, < 10 CFU/g viable *Yarrowia lipolytica* cells, and ≤ 10 CFU/g coliforms.

The total saturated, monounsaturated, and polyunsaturated fatty acid composition of *Candida lipolytica* (synonymous to *Yarrowia lipolytica*) was determined to be 13.63, 63.36, and 23.01% (of total fatty acids), respectively (measured via gas chromatography mass spectrometry).[21] The specific fatty acids observed can be found in Table 4. In addition, the nutrient, amino acid, and mineral composition of a *Yarrowia lipolytica* sample can be found in Table 5.

Yarrowia lipolytica can accumulate lipids to levels > 50% of cell dry weight.[34] These lipids consist mostly of triglycerides and steryl esters. This accumulation, however, depends on multiple factors including environmental conditions, temperature, pH, production of secondary metabolites, nutrient limitation, and microorganism physiology.

Yeast Extract

According to a supplier, a Yeast Extract derived from several different yeast species (*Candida magnoliae, Candida oleophila, Candida saitoana, Debaryomyces nepalensis, Metschnikowia agaves, Metschnikowia reukaufii, Metschnikowia pulcherrima, Pichia anomala, Pichia heedii, Picha minuta, and Pichia naganishii*) contained 10-53% sugars, 38-39% mineral ashes, and 7-60% proteins.[20] The sum of heavy metals in these extracts were reported to be < 20 ppm.

USE

Cosmetic

The safety of the cosmetic ingredients addressed in this assessment is evaluated based on data received from U.S. Food and Drug Administration (FDA) and the cosmetics industry on the expected use of these ingredients in cosmetics and does not cover their use in airbrush delivery systems. Data are submitted by the cosmetic industry via the FDA's Voluntary Cosmetic Registration Program (VCRP) database (frequency of use) and in response to a survey conducted by the Personal Care Products Council (Council) (maximum use concentrations). The data are provided by cosmetic product categories, based on 21CFR Part 720. For most cosmetic product categories, 21CFR Part 720 does not indicate type of application and, therefore, airbrush application is not considered. Airbrush delivery systems are within the purview of the US Consumer Product Safety Commission (CPSC), while ingredients, as used in airbrush delivery systems, are within the jurisdiction of the FDA. Airbrush delivery system use for cosmetic application has not been evaluated by the CPSC, nor has the use of cosmetic ingredients in airbrush technology been evaluated by the FDA. Moreover, no consumer habits and practices data or particle size data are publicly available to evaluate the exposure associated with this use type, thereby preempting the ability to evaluate risk or safety.

According to 2023 VCRP survey data, Yeast Extract is reported to be used in 398 formulations (343 leave-on formulations and 55 rinse-off formulations; Table 6).[35] All other in-use ingredients are reported to be used 81 formulations or less. The results of the concentration of use survey conducted by the Council indicate Galactomyces Ferment Filtrate has the highest concentration of use in a leave-on formulation; it is used at up to 90.7% in moisturizing products (not spray).[36] Based on VCRP data and concentration of use survey results, 18 yeast-derived ingredients are reported to be used; the 38 ingredients not in use according to the VCRP and industry survey are listed in Table 7.

Incidental ingestion of several of these ingredients may occur as they are reported to be used in lipstick formulations (e.g., Saccharomyces Ferment is used in lipstick formulations at 0.00013%). These ingredients are also reported to be used in products that may result in mucus membrane (e.g., Saccharomyces Ferment Filtrate is used at up to 0.038% in feminine deodorants) and eye exposure (e.g., Galactomyces Ferment Filtrate is used in eye lotions at up to 37.5%). Saccharomyces Lysate Extract is used at up to 0.067% in baby lotions/oils/powders/creams.

Some of these ingredients are used in cosmetic sprays and powders, and could possibly be inhaled; for example, Saccharomyces Ferment Filtrate and Yeast Extract are used in colognes and toilet waters at 0.065% and Galactomyces Ferment Filtrate is reported to be used at 1.1% in face powders. In practice, as stated in the Panel's respiratory exposure resource document (https://www.cir-safety.org/cir-findings), most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and tracheobronchial regions and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount. Conservative estimates of inhalation exposures to respirable particles during the use of loose powder cosmetic products are 400-fold to 1000-fold less than protective regulatory and guidance limits for inert airborne respirable particles in the workplace.

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

The yeast-derived ingredients reviewed in this report are not restricted from use in any way under the rules governing cosmetic products in the European Union.[37]

Non-Cosmetic

Yeasts are commonly used worldwide in the food and beverage industry, mainly in baking and alcohol production as a fermentative agent.[38] The use/presence of several of the species reviewed in this report in foods, their GRAS status, their Qualified Presumption of Safety (QPS) status (as designated by the EFSA), and information regarding other non-cosmetic uses of these species are provided in Table 8. Specifications required for the GRAS ingredients derived from *Saccharomyces cerevisiae* are described in the Composition and Impurities section of this report.

TOXICOKINETIC STUDIES

Dermal Absorption

Details of the in vitro dermal absorption studies summarized below can be found in Table 9.

Several in vitro dermal absorption assays were performed according to Organisation for Economic Cooperation and Development test guideline (OECD TG) 428 on 30% emulsions of Metschnikowia Agaves Extract, Pichia Anomala Extract, Pichia Heedii Extract, Pichia Minuta Extract, a Yeast Extract derived from *Candida saitoana*, and a Yeast Extract derived from *Metschnikowia reukaufii*.[20] Dermal absorption in these studies ranged from 0.2 to 4.6% of the applied dose 24 h after application.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

Details on the acute toxicity studies summarized below can be found in Table 10.

Median lethal doses (LD_{50}s) of > 2000 mg/kg were predicted in 3T3 neutral red uptake assays performed using Pichia Minuta Extract and Yeast Extract (derived from *Pichia naganishii*).[39] An LD_{50} of > 2000 mg/kg was established in rats in acute dermal toxicity assays at a test concentration of 49.5% *Saccharomyces cerevisiae* cell wall in hydrated sodium calcium aluminosilicate (HSCAS) and a *Saccharomyces cerevisiae* extract (in water).[2,4] Similarly, no toxicity was observed in acute oral toxicity assays performed in mice using a *Galactomyces* ferment filtrate (up to 60,000 mg/kg) or in rats with a yeast hydrolysate obtained from *Saccharomyces cerevisiae* (5000 mg/kg bw), 49.5% *Saccharomyces cerevisiae* cell wall (2000 mg/kg bw), a fermentate powder derived from *Saccharomyces cerevisiae* (2000 mg/kg), or *Candida oleophila* strain O (2.3 - 3.8 x 10^8 CFU).[4,31,40-42] Acute inhalation toxicity was evaluated in rats using 49.5% *Saccharomyces cerevisiae* cell wall (2.09 mg/l).[4] The median lethal concentration (LC_{50}) was determined to be > 2.09 mg/l. *Candida oleophila* strain O was not toxic at 1.2 - 5.2 x 10^8 CFU in an inhalation study or 1.1 - 2.0 x 10^7 CFU in a parenteral study performed in rats.[42] No adverse effects were observed in an acute toxicity assay performed in mice inoculated with live *Pichia pastoris* cells (in saline; 1 × 10^6 CFU).[43]

Repeated-Dose Toxicity Studies

Details on the repeated-dose oral toxicity studies summarized below can be found in Table 11.

No significant adverse effects were noted in a 14-d assay in which rats (5/sex/group) were orally administered 1000 mg/kg bw/d yeast hydrolysate derived from *Saccharomyces cerevisiae* (method of oral administration and vehicle not stated).[31] In a different 14-d study, *Kluyveromyces marxianus* extracts (strains A4 and A5; 1.0 x 10^6 CFU/ml or 1.0 x 10^8 CFU/ml; in sterilized saline) were orally administered to female mice (6/group; method of oral administration not stated).[44] Statistically significant lower spleen to body ratios and liver to body ratios were noted in mice treated with the high concentration of the A5 strain, and the low concentration of the A4 strain, respectively. No other adverse effects were observed. *Phaffia rhodozyma* extract (up to 1000 mg/kg) in corn oil was given to rats (6/sex/group), via gavage, for 28 d.[45] The no-observed-adverse-effect-level (NOAEL) was determined to be > 1000 mg/kg. Fermentate powder derived from *Saccharomyces cerevisiae* (in methylcellulose and water) was given to rats (20/sex/group) in a 90-d study (rats given up to 1500 mg/kg bw/d; via gavage), and a 1-yr study (rats given up to 800 mg/kg bw/d; via gavage).[41] All administrations were performed via gavage. The NOAELs for the 90-d and 1-yr study were determined to be 1500 mg/kg bw/d and 800 mg/kg bw/d (the highest dose administered in each study), respectively.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY STUDIES

No relevant developmental and reproductive toxicity studies on the yeast-derived ingredients evaluated in this report were found in the published literature, and unpublished data were not submitted.

GENOTOXICITY STUDIES

Details on the genotoxicity studies summarized below can be found in Table 12.

Negative results were obtained for Ames assays performed on *Galactomyces* ferment filtrate (in water; up to 10,000 µg/plate), 90% yeast (*Saccharomyces cerevisiae*) cell wall (in HSCAS; up to 3500 µg/plate), *Phaffia rhodozyma* extract (in acetone; up to 5000 µg/plate), a trade name mixture containing 49% Phaffia Rhodozyma Extract (in water; up to 5000 µg/plate), Pichia Minuta Extract (concentration not stated), fermentate powder derived from *Saccharomyces cerevisiae* (in methylcellulose and water; up to 5000 µg/plate), a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate (in water; up to 5000 µg/plate), *Candida oleophila* strain O (concentration not stated), and a Yeast Extract derived from *Pichia naganishii* (concentration not stated).[4,39,41,45-48] Negative results were also obtained in mammalian cell gene mutation assays performed using a fermentate powder derived from *Saccharomyces cerevisiae* (in methylcellulose and water; up to 5000 µg/plate) and *Candida oleophila* strain O (concentration not stated). No mutagenicity was observed in micronucleus assays performed using Pichia Minuta Extract (concentration not stated) and Yeast Extract derived from *Pichia naganishii* (concentration not stated). Mammalian bone marrow chromosomal assays were performed using a *Phaffia rhodozyma* extract (in corn oil; up to 2000 mg/kg bw/d; performed in 3 male mice/group; oral administration) and 90% yeast (*Saccharomyces cerevisiae*) cell wall (in HSCAS; up to 2000 mg/kg bw/d; performed 28 mice/sex/group; via gavage). Both test substances were considered to be non-clastogenic.

CARCINOGENICITY STUDIES

No relevant carcinogenicity studies on the yeast-derived ingredients evaluated in this report were found in the published literature, and unpublished data were not submitted.

ANTI-CARCINOGENICITY STUDIES

In Vitro

Saccharomyces cerevisiae

Treatment with *Saccharomyces cerevisiae* resulted in the growth inhibition or apoptosis of several cancer cell types in multiple anti-carcinogenicity assays.[49-52] Cell lines that were inhibited by *Saccharomyces cerevisiae* include human metastatic breast cancer cells (MCF-7 and ZR-75-1), non-metastatic breast cancer cells (HCC70), squamous cell carcinoma of the tongue (SCC-4), adenocarcinomas of the colon (Caco-2, DLD1, and HCT116; concentrations not reported), and cervical cancer cells (HeLa; up to 1000 µg/ml yeast cells).

OTHER RELEVANT STUDIES

Anti-Inflammatory Effects

The following study is included as it may help in providing information regarding dermal irritation/allergy alleviation following exposure to Saccharomyces Ferment, when derived from *Saccharomyces cerevisiae*.

Saccharomyces cerevisiae

The anti-inflammatory properties from a dried fermentate derived from *Saccharomyces cerevisiae* was evaluated using a single-blind, placebo-controlled assay (n = 12 subjects). To induce inflammation, 0.01 ml of a dilute solution of histamine was applied to the forearm of each subject, and a scratch was performed using a sterilized lancet. One min after the scratch, the histamine solution was removed, and 0.01 ml dried fermentate (0.1 g/ml) was applied to the site. After 1 min, the dried fermentate was removed, and laser Doppler probes evaluated skin sites (evaluation for 10 min). Doppler probe measured parameters included the time to maximum blood perfusion (T_{max}), and the slope of the curve generated during the resolution phase over time, as a measure of the speed of resolution. This same procedure was performed on the other forearm using saline (negative control) instead of dried fermentate. After probes were removed, each subject was asked to score the level of itching on each skin site using a 100 mm Visual Analogue Scale. Among the 12 test subjects, the observed average time to T_{max} on sites treated with dried fermentate were significantly shorter than sites treated with saline ($p < 0.05$). In addition, the slope of the curve after T_{max} was significantly lower compared to saline treated site s ($p < 0.05$), indicating that treatment with dried fermentate resulted in a faster process of inflammation resolution.

Immunomodulatory Effects

The following studies are included as they may be helpful in providing information regarding potential allergenicity/ hypersensitivity of the yeast-derived ingredients evaluated in this report.

Candida pseudotropicalis (synonymous to *Kluyveromyces fragilis*), *Geotrichum candidum* (synonymous to *Galactomyces candidus*), and *Saccharomyces cerevisiae*

Immunological cross-reactivity of several yeast species (*Candida albicans*, *Candida pseudotropicalis*, *Candida krusei*, *Candida parapsilosis*, *Candida tropicalis*, *Candida guilliermondii*, *Candida humicola*, *Candida norvegica*, *Candida utilis*, *Cryptococcus albidus*, *Geotrichum candidum, Pitryosporum pachydermatis, Pitryosporum ovale, Rhodotorula minuta, Rhodotorula rubra, Saccharomyces cerevisiae, Torulopsis glabrata*, and *Trichosporon cutaneum*) was evaluated.[53] Cross-reactive components of yeast extracts were measured via an enzyme immunoassay using rabbit anti-*Candida albicans* antiserum. Results were expressed relative to the absorbance observed with *Candida albicans* extract. Significant cross-reactivity was only observed between Candida species. Skin prick tests were performed in 67 atopic patients using whole cell and disrupted cell extracts several yeast species including *Saccharomyces cerevisiae*. Whole cell and disrupted cell extracts of *Saccharomyces cerevisiae* resulted in positive results in 41 and 31% of patients, respectively.

Pichia pastoris

A delayed-type hypersensitivity test was performed in female BALB/c mice to evaluate cell-mediated immunity to live *Pichia pastoris* cells.[43] Four groups of 5 adult mice were anesthetized and abdominal skin was shaved. Approximately 50% of the stratum corneum was removed, and *Pichia pastoris* cells (2×10^8 CFU in 50 µl sterile saline) were applied epicutaneously. Vehicle group mice received applications of 50 µl sterile saline on stratum corneum-removed skin. Another group of control mice consisted of shaved animals without disruption of the stratum corneum and were used to evaluate baseline measures. Seven days after administration, ear thickness was measured with a micrometer. To achieve the efferent phase of the delayed-type hypersensitivity response, mice were challenged with inoculation into the ears with heat-killed *Pichia pastoris* cells (1×10^7 CFU). Swelling was calculated by subtracting the ear thickness 24 h after the challenge from the baseline thickness. Results between control, vehicle-control, and *Pichia pastoris*-treated groups were similar, indicating that *Pichia pastoris* did not induce a cell-mediated immune response.

Saccharomyces cerevisiae

Forty-seven patients with inhalant allergy to fungi were tested for allergic sensitivity to baker's yeast (*Saccharomyces cerevisiae*).[16] Baker's yeast extract and purified enolase obtained from baker's yeast were each formulated at concentrations of 1 and 10 mg/ml in a diluent of 50% glycerin in sterile saline. Skin prick testing was performed using both the baker's yeast extract and purified enolase on each of the 47 patients. Non-fungi allergic control subjects (10 non-allergic subjects

and 10 grass-pollen and/or mite-allergic patients) were subjected to skin prick tests with baker's yeast extract. Wheal sizes were recorded 15 min following skin prick. Clear wheal and flare skin reactions to baker's yeast extract were observed at both test concentrations (wheal sizes of at least 3 mm) in fungi-allergic patients. No skin reactions were seen at either test concentration in control subjects that were not reported to have fungi allergy. Twenty-three of the fungi-allergic patients showed an allergic response to baker's yeast enolase. Sera from all 47 fungi-allergic patients were subjected to radioallergosorbent testing (RAST) using both baker's yeast extract and enolase. Sera from 10 of these patients were RAST-negative to baker's yeast extract and enolase, and 5 other sera were considered doubtful positives. Thirty-two patients were RAST-positive, 22 of which showed RAST uptakes with enolase that were equal to, or higher than, the uptakes recorded with baker's yeast extract. Skin prick tests for these 32 RAST-positive patients revealed that in 25 subjects, wheal sizes to enolase were equal to, or greater than, wheal sizes recorded for baker's yeast extract.

In a different study, the potential sensitizing effects of a *Saccharomyces cerevisiae* extract was evaluated in 449 patients (226 with atopic dermatitis, 50 with allergic rhinitis and/or asthma, and 173 non-atopic controls) via a skin prick test.[54] Skin prick tests were performed in duplicate, and the results were evaluated after 15 min. Serum samples were taken for total serum immunoglobulin E (IgE) determinations. Twenty percent of patients (92) had positive skin prick tests to the extract. Of these subjects, 85 were atopic dermatitis patients, 4 had allergic rhinitis and/or asthma, and 3 were nonatopic controls. There was a significant correlation between the severity of eczema and frequency of positive skin test results to *Saccharomyces cerevisiae*. Patients with moderate to severe dermatitis displayed positive skin prick test reactions significantly more frequently than allergic rhinitis/asthma patients or nonatopic controls ($p < 0.001$). In addition, a parallel skin reactivity assay was performed with other yeasts and common allergens. Parallel skin reactivity was observed with yeasts (*Pitryosporum ovale* and *Candida albicans*), molds, and animal dander, but not with pollen or dust mites. In addition, a significant correlation between total serum IgE and positive skin prick test results with *Saccharomyces cerevisiae* was seen ($r = 0.53$, $p < 0.001$).

Allergens of *Saccharomyces cerevisiae* were evaluated via an IgE-immunoblotting assay performed on 83 subjects.[55] Sixty-three of these patients were previously diagnosed with atopic dermatitis with positive skin prick tests or RAST for *Saccharomyces cerevisiae*, and 7 subjects were diagnosed with atopic dermatitis, but did not have positive skin prick tests or RAST for *Saccharomyces cerevisiae*. The remaining 13 subjects were non-atopic controls. A disrupted whole-body extract of *Saccharomyces cerevisiae* was used for evaluation. Forty-one atopic subjects were positive in the IgE immunoblotting assay, revealing 22 IgE stained bands (10 bands represented immediate allergens, and 12 bands represented minor allergens). In 39% of positive subjects, staining of the 48 kD band was observed. Non-atopic (control-subject serum) and sera from atopic patients with negative skin prick tests to *Saccharomyces cerevisiae* were IgE negative in this experiment.

IgE, IgA, and IgG responses to common yeasts, including *Candida albicans*, *Candida utilis*, *Cryptococcus albidus*, *Rhodotorula rubra*, and *Saccharomyces cerevisiae*, were evaluated via an immunoblotting assay.[56] In addition, the cross-reactivity of their IgE-binding components were also evaluated. Twenty atopic subjects with asthma, allergic rhinitis, or atopic dermatitis, were included in the study (16 patients skin prick test-positive to yeast, 4 were not and served as controls). IgE immunoblotting revealed IgE-binding bands in all species (*Candida albicans* (11 bands), *Candida utilis* (8 bands), *Saccharomyces cerevisiae* (5 bands), *Rhodotorula rubra* (5 bands), and *Cryptococcus albidus* (4 bands)). The 46-kDa band was shared by all 5 yeasts, and the 13-kDa band was shared by 4 yeasts. Prominent IgE binding was seen to a 46-kDa band of *Candida albicans* (7 subjects), *Candida utilis* (5 patients), and *Saccharomyces cerevisiae* (1 patient). Strong IgG responses were observed against *Saccharomyces cerevisiae* (19 patients had a response; 14 patients had a response to *Saccharomyces cerevisiae* mannans) and *Candida albicans* (18 patients had a response; 17 patients had a response to *Candida albicans* mannans). The corresponding patient numbers in IgA immunoblotting were 17 (*Candida albicans*), 17 (*Candida albicans* mannans), 15 (*Saccharomyces cerevisiae*), 7 (*Saccharomyces cerevisiae* mannans), 5 (*Rhodotorula rubra*), 11 (*Cryptococcus albidus*), and 2 (*Cryptococcus albidus* mannans). An IgA response to the 20-kDa band of *Saccharomyces cerevisiae* was observed in 12 patients.

Pulmonary Toxicity

The following studies are included in this report as they may be helpful in evaluating the inhalation toxicity potential of yeast-derived ingredients.

<u>*Geotrichum candidum* (synonymous to *Galactomyces candidus*)</u>

The cause of allergic alveolitis was evaluated in 12 Australian patients.[57] The houses of all patients were evaluated and inspected. Extensive wood decay was found in 10/12 houses, while 4/12 also had obvious fungal growth on damp walls. Twelve fungal species were observed in homes, including *Geotrichum candidum* (synonymous to *Galactomyces candidus*). Precipitin tests were performed on the 12 patients, along with 14 controls, using freeze-dried fungal extracts (30 mg/ml) of the 12 observed fungal species, in addition to several other species and allergens. If results were negative, tests were repeated using serum that had been concentrated to 20% of the original volume by desiccation. Six of the 12 patients exhibited positive precipitins to one or more of the fungi when unconcentrated serum was used. Nine of 12 patients displayed positive precipitins with concentrated serum (2 positive reactions to *Geotrichum candidum* extract). No precipitins were found to any of the fungal groups in control subjects. Skin prick tests were performed in all patients (number of control subjects not specified) using freeze-dried fungal extracts (10 mg/ml) and other allergens. One patient displayed a positive reaction to

Geotrichum candidum extract. Inhalation tests were performed with 3 control subjects and 6 patients with alveolitis using solutions of nebulized yeast (*Serpula lacrymans*, *Geotrichum candidum*, and *Aspergillus fumigatus*; 1 mg/ml). Measurements (spirometry and single breath diffusion capacity) were taken every 15 min for the first hour, and every 30 min for at least 8 h. No immediate positive responses were observed; however, positive late responses were obtained to *Serpula lacrymans* (3 positive reactions), *Geotrichum candidum* (2 positive reactions), and *Aspergillus fumigatus* (2 positive responses). Relocation of patients resulted in improvement of symptoms in all cases.

Effect on Pigmentation

The following study is included in this report as it may be helpful in evaluating the potential anti-pigmentation effects of yeast-derived ingredients.

Galactomyces Ferment Filtrate

The effect of Galactomyces Ferment Filtrate on melanization was evaluated in vitro.[58] Cultured normal human melanocytes were exposed to Galactomyces Ferment Filtrate in concentrations of 15, 20, and 30%. Galactomyces Ferment Filtrate at a concentration of 15% did not affect melanocyte viability; however, concentrations of 20 and 30% reduced melanocyte viability by 20 and 50%, respectively. Human melanoma cells and normal human melanocytes (derived from both light and dark skin) were treated with either 5 or 10% Galactomyces Ferment Filtrate, every other day, and evaluated for melanin content. In melanoma cells, a 60% reduction in melanin was noted after treatment with both 5 and 10% Galactomyces Ferment Filtrate, within 12 d. In normal human melanocytes, melanin was reduced by 30 and 55%, after treatment with 5 and 10% Galactomyces Ferment Filtrate, respectively, within 25 d. Galactomyces Ferment Filtrate appeared slightly more effective on normal human melanocytes from dark skin as opposed to light skin. According to this study, Galactomyces Ferment Filtrate did not influence the expression of tyrosinase related protein 1 or premalanosome protein 17, and had a minimal effect on reducing the expression of tyrosinase. In order to determine the mechanism of action of Galactomyces Ferment Filtrate, the effect of Galactomyces Ferment Filtrate on the expression of nuclear factor erythroid 2-related factor 2 (Nrf2) and glutathione S-transferase (GST) was evaluated in human melanoma cells. Galactomyces Ferment Filtrate (10%) increased the expression of Nrf2, over 70%, within 16 d. In addition, an 8-d treatment of 10% Galactomyces Ferment Filtrate on human melanoma cells increased the expression of GST.

The effect of three Galactomyces Ferment Filtrate-containing skin care products (concentration of Galactomyces Ferment Filtrate in product not stated) on hyperpigmented spots (as induced by skin aging) was evaluated in 86 volunteers over a 1-yr treatment period.[59] An original evaluation was performed in 1999. In 2010 (11 yr later), subjects were instructed to apply all three products (2 essence preparations and 1 cream preparation) twice daily for 1 yr. Skin was evaluated at 2, 8, and 12 mo during this period. Hyperpigmented spots were significantly aggravated when evaluated in 2010 prior to the 12 mo treatment with Galactomyces Ferment Filtrate-containing products ($p < 0.01$). Hyperpigmentation gradually decreased during the 12-mo treatment period, and eventually recovered to a level close to that in 1999.

Saccharomyces cerevisiae

The effect of a natural yeast extract isolated by ethanol precipitation from *Saccharomyces cerevisiae* on melanogenesis was evaluated in an in vitro assay.[60] To evaluate the melanin synthesis inhibition, B16F10 cells (melanocytes) were exposed to the extract (50, 100, and 200 µg/ml) for 72 h. The test substance inhibited melanin synthesis from α-melanocyte-stimulating-hormone (α-MSH)-stimulated B16F10 cells in a dose-dependent manner. Melanin synthesis was also evaluated in melanocytes co-cultured with human keratinocytes (HaCaT), and treatment with the same test substance at concentrations of 50, 100, and 500 µg/ml. Melanin synthesis in these co-cultured melanocytes was also decreased in a dose-dependent manner. The inhibitory effect of the same *Saccharomyces cerevisiae* extract on tyrosinase was examined by a cell-free tyrosinase assay with mushroom tyrosinase, and by an intracellular tyrosinase assay in B16F10 cells. Cells were treated with the test substance (50, 100, and 500 µg/ml), or the positive control, arbutin. The test substance decreased the activity of intracellular tyrosinase in a dose-dependent manner, but had no direct inhibitory effect on tyrosinase itself. The positive control showed significant inhibitory effect on tyrosinase activity in the cell-free assay, in a dose-dependent manner.

Cytotoxicity

Cellular viability assays were performed using a trade name mixture containing 49% Phaffia Rhodozyma Extract and a trade name mixture containing 25% Saccharomyces Lysate Extract (both test substances tested at concentrations of 0.1 and 0.01%).[61,62] Assays were performed using normal human dermal fibroblasts (24 h incubation). Neither test substance was considered to be cytotoxic.

DERMAL IRRITATION AND SENSITIZATION STUDIES

Details of the irritation, sensitization, and phototoxicity/photosensitization studies summarized below are provided in Table 13. In addition, Table 14 provides an overview of the available sensitization data per ingredient, along with an indication as to whether the studies assess key events (KE) in the adverse outcome pathway (AOP) for skin sensitization.[63] Notations are also provided if guinea pig maximization tests, Buehler tests, or human repeated insult patch tests (HRIPTs) were performed.

In vitro dermal irritation assays yielded negative results (majority of studies performed were EpiDerm™ assays).[2,13,64-70] Tests were performed using a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall, a trade name mixture containing 49% Phaffia Rhodozyma Extract, a powdered *Saccharomyces cerevisiae* extract, trade name mixtures containing 1.25, 3, and 4.5% Saccharomyces Cerevisiae Extract, a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, and trade name mixtures containing 10% and 98% Saccharomyces Lysate Extract, and all materials were tested as supplied. Slight irritation was observed in an irritation assay performed in rabbits using a mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall in 10% HSCAS (tested at 55% in water under semi-occlusive conditions).[4] No irritation as observed in a primary dermal irritation assay in which a non-cosmetic product containing 57% *Candida oleophila* strain O was applied to the skin of rabbits.[39] In dermal patch tests in humans, the following were tested and found to be non-irritating: a *Galactomyces* ferment filtrate (tested neat; multiple patch test); a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall (tested neat; single patch test); Metschnikowia Agaves Extract, Pichia Anomala Extract, Pichia Heedii Extract, Pichia Minuta Extract, and Yeast Extract derived from *Candida mangoliae, Candida saitoana*, *Metschnikowia pulcherrima*, and *Metschnikowia reukaufii* (all tested at 15% aq.; single patch tests); a cosmetic formulation containing 1% *Saccharomyces cerevisiae* extract (tested neat; single patch test).[13,20,71,72] In a 4-wk use study, no irritation was observed when subjects applied a cream containing 100% Lipomyces Lipid Bodies to the hands and face.[25]

No sensitization potential was observed in several in chemico/in vitro sensitization assays. Direct peptide reactivity assays (DPRA; assesses KE1 in the AOP) were performed using Phaffia Rhodozyma Extract (100 mM in acetonitrile) and trade name mixture containing 24% Saccharomyces Ferment Lysate Filtrate (100 mM acetonitrile).[73,74] KeratinoSens™ assays (assess KE2 in the AOP) were performed using a trade name mixture containing 8 - 10% Hydrolyzed Saccharomyces Cell Wall, a trade name mixture containing 0.4% Hydrolyzed Yeast, a trade name mixture containing 49% Phaffia Rhodozyma Extract, Pichia Minuta Extract, a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, and Yeast Extracts derived from *Candida magnoliae*, *Metschnikowia reukaufii,* and *Pichia naganishii* (majority of test substances tested at up to 2000 µM).[13,20,39,74-76] Human cell line activation tests (h-CLAT; assesses KE3 in the AOP) were performed using Hydrolyzed Yeast (up to 5000 µg/ml) and Yeast Extract (derived from *Pichia naganishii* (concentration tested not stated)).[39,75] A U937 cell line activation test (U-SENS™; also assesses KE3 in the AOP) was performed using Pichia Minuta Extract (concentration tested not stated).[39]

Local lymph node assays (LLNA; assess KE4 in the AOP) were performed in mice for *Saccharomyces cerevisiae* extract at concentrations of up to 50%.[2] In one assay, the test substance was considered to be sensitizing at concentrations > 10%; however, in four other assays performed according to the same procedure, the test substance was considered to be non-sensitizing. In guinea pig studies, no sensitization was observed in a guinea pig maximization test (GPMT) of *Galactomyces* ferment filtrate (tested neat),[77] and no sensitization was observed in a Buehler assay performed using a mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall in 10% HSCAS (tested at 49.5% in water and carboxymethylcellulose).[4]

Human studies were performed for several of the yeast-derived ingredients. HRIPTs of a skincare product containing 1.485% Galactomyces Ferment Filtrate (tested neat; n = 104), a facial treatment essence containing 92.675% Galactomyces Ferment Filtrate (tested neat; (n = 100)), a trade name mixture containing 0.4% Hydrolyzed Yeast (tested at 0.01%; final test concentration of Hydrolyzed Yeast: 0.00004%; n = 51), a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall (tested neat; n = 50), a cream containing 0.0135% Saccharomyces Ferment Lysate Filtrate (n = 52), a trade name mixture containing 2% Saccharomyces Ferment Lysate Filtrate (tested neat; n = 105), a cream containing 0.028% Saccharomyces Lysate Extract (tested neat; n = 50), and a trade name mixture containing 25% Saccharomyces Lysate Extract (tested at 10% in water; final test concentration of Saccharomyces Lysate Extract: 2.5%; n = 50); a lotion containing 0.0045% Yeast Extract (n = 52), 15% aq. Metschnikowia Agaves Extract (n = 112), Pichia Anomala Extract (n = 100 and n = 104), Pichia Heedii Extract (n = 106), Pichia Minuta Extract (n = 107), a Yeast Extract derived from *Candida saitoana* (n = 112), and a Yeast Extract derived from *Metschnikowia reukaufii* (n = 104) were negative for sensitization.[13,20,78-85]

No phototoxicity was observed in EpiDerm™ assays performed using a trade name mixture containing 49% Phaffia Rhodozyma Extract or a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate (both test substances tested at up to 10%).[86,87] Similarly, no phototoxicity or photosensitization was observed in assays performed on animals using *Galactomyces* ferment filtrate (tested neat; n = 3 rabbits in phototoxicity assay, n = 10 guinea pigs/group in photosensitization assay).[88,89]

OCULAR IRRITATION STUDIES

Details on the ocular irritation studies summarized below can be found in Table 15.

Several in vitro assays were performed. The following test substances were predicted to be either minimally or non-irritating in in vitro ocular assays: a facial treatment essence containing 92.675% *Galactomyces* ferment filtrate, a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall, a trade name mixture containing 49% Phaffia Rhodozyma Extract, Pichia Minuta Extract (concentration not stated), several trade name mixtures containing Saccharomyces Cerevisiae Extract (up to 20%), a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, two trade name mixtures containing Saccharomyces Lysate Extract (up to 98%), and Yeast Extract derived from *Pichia naganishii*.[2,39,64-70,90]

No irritation was observed in an ocular irritation assay performed in rabbits using *Galactomyces* ferment filtrate (tested neat).[91] Minimal irritation was observed in an ocular irritation assay performed in rabbits using a mixture containing 90% *Saccharomyces cerevisiae* cell wall in HSCAS and in an assay performed in rabbits using a non-cosmetic product containing 57% *Candida oleophila* strain O.[4,39] Resolvable irritation was observed in rabbits treated with an undiluted powdered *Saccharomyces cerevisiae* extract.[2]

CLINICAL STUDIES

Case Reports

Case reports were found in the literature describing infection relating to several of the yeast species reviewed in this report.[92-115] These reports, however, were found in immunocompromised or post-surgical patients; therefore, their relevancy to cosmetic safety is unlikely.

Candida oleophila

During a pilot-plant production trial of a product containing *Candida oleophila* strain O (as an active ingredient at 57% by weight), 3 out of 6 workers not wearing personal protective equipment reported clinical symptoms of a respiratory reaction.[42] No adverse dermal effects were observed.

Saccharomyces cerevisiae

A 29-yr-old woman presented to the hospital with multiple severe anaphylactic reactions induced by food.[116] The patient reported a pollen and animal dander allergy, and previous anaphylactic reactions after exposure to contrast media, beer, wine, spaghetti Bolognese sauce, pasta, and bread. Skin prick tests revealed positive results for soya, various nuts and seeds, anthocyanin, and beer malt containing barley. The next anaphylactic reaction took place following ingestion of a meal consisting of industrial-made olive sauce, pasta, and feta cheese. The patient experienced severe allergic symptoms including angioedema of the throat, difficulty breathing, and near loss of consciousness, and was treated in the emergency department. Three wk after the reaction, the patient was examined using skin prick tests and serum allergen-specific IgE/inhibition tests. Various yeasts and molds were tested as well as 2 pasta sauces, individual sauce ingredients, commercial yeast extract preparations, and wines. Skin prick and serum IgE test results were positive to several molds (*Cladosporium herbarum*, *Alternaria alternata*, *Aspergillus fumigatus*, and *Penicillium notatum*), baker's yeast (*Saccharomyces cerevisiae*), *Malassezia furfur*, champignon and the 2 pasta sauces, the yeast ingredient, and a food-quality yeast extract.

A 33-yr-old with a history of allergic rhinoconjunctivitis with exercise-induced asthma reported experiencing episodes of anaphylaxis with no associated exercise over a period of 3 yr.[117] These reactions were successfully treated with epinephrine. The patient related the episodes to ingestion to beer, chips, olives, and wine. Skin prick tests with common aeroallergens, beer extracts, wine, yeast (including several *Saccharomyces cerevisiae* extracts), cereal extracts, and fruits were performed. Results were positive with beer extract, *Saccharomyces cerevisiae* extracts, *Penicillium nalgiovense*, and mushrooms. A sodium dodecyl sulfate-polyacrylamide gel electrophoresis immunoblotting assay was performed with several beer extracts, *Saccharomyces cerevisiae* extract, and the patient's serum. The main IgE-reactive bands detected in the beer extracts were 97 kDa, 80 kDa, 55 kDa, 40 kDa, 32 kDa, and 17 kDa. In the *Saccharomyces cerevisiae* extract, a high intensity IgE-binding zone was observed between 100 kDa and 29 kDa, and a band around 17 kDa. In order to determine whether *Saccharomyces cerevisiae* was the allergenic source of IgE-reactive proteins detected in beer extracts, an immunoblotting-inhibition assay was performed using a Trappist-style beer extract in the solid phase and beer extracts and *Saccharomyces cerevisiae* extracts as inhibitors. Both beer extracts and *Saccharomyces cerevisiae* extracts produced total inhibition of IgE-binding in the Trappist-style beer extract.

A 25-yr-old woman was admitted to the hospital with a dry cough, low-grade fever, and focal patchy shadow of pulmonary infiltrates.[118] The patient had no previous history of atopic diseases. Because *Saccharomyces cerevisiae* was detected in patient sputum, eosinic bronchitis caused by *Saccharomyces cerevisiae* was suspected. Fungal antigenic solutions were prepared by culturing fungus on medium containing 0.5% yeast extract. Skin tests with the fungal antigens were performed via intradermal injection of the antigen solution (1 mg/ml). Reactions to the injections were observed 15 min and 48 h post-administration. The patient displayed an immediate positive skin reaction to *Saccharomyces cerevisiae*, but both the immediate and delayed skin reactions were negative for *Penicillin janthinellum* as a control. After 7 d of beclomethasone dipropionate inhalation therapy, the patient's symptoms improved, and *Saccharomyces cerevisiae* was no longer present in sputum. Three mo later, the patient was readmitted for bronchoprovocation testing using *Saccharomyces cerevisiae* and *Penicillin janthinellum* antigens. Antigen solutions were administered via a nebulizer. Test results were negative following *Penicillin janthinellum* antigen exposure, but positive following *Saccharomyces cerevisiae* exposure. The patient exhibited a coughing attack, high fever, and ticklish throat within 15 min of exposure. Serum C-reactive protein and sputum eosinophils were increased on the day after provocation testing with *Saccharomyces cerevisiae* antigen. Symptoms disappeared 3 d after testing.

A 48-yr-old bakery worker presented with repeated episodes of hydrorrhea, sneezing, nasal obstruction, wheezing, spasmodic cough, and dyspnea, with symptoms occurring 1-2 h after the start of a workday.[119] Treatment with budesonide and salbutamol was started; however, symptoms were not fully controlled. Skin prick tests were performed using extracts of dehydrated yeast in dry powder form (*Saccharomyces cerevisiae*), conventional wet yeast (*Saccharomyces cerevisiae*), a

commercial mixture of baking additives, a battery of inhalant allergies and pollens, flours (wheat, soybean, and barley), and alpha-amylase. Yeast extracts were evaluated at dilutions of 10^{-4} – 10^{-2}. Negative reactions were observed for all non-yeast test substances and the 10^{-4} and 10^{-3} dilutions of the yeast extracts (both wet and dry); however, positive responses to the wet and dry yeast extracts were observed at the 10^{-2} dilution. In addition, baseline peak expiratory flow rates (PEFR) were evaluated when the patient was at the workplace versus away from the workplace. On the patient's workdays the PEFR measurements showed significant decreases from baseline values (>25%). During time away from the workplace, PEFR values did not fall more than 20%. During a nonspecific bronchial provocation test using a dry *Saccharomyces cerevisiae* extract (dilution of 10^{-3}), a drop in forced expiratory volume and shortness of breath/wheezing was observed. These symptoms were not observed when the extract was tested at a 10^{-4} dilution. The patient was diagnosed with occupational asthma caused by *Saccharomyces cerevisiae* sensitization, and began to use conventional wet yeast without symptoms.

SUMMARY

The safety of 56 yeast-derived ingredients as used in cosmetics is reviewed in this safety assessment. According to the *Dictionary*, the majority of these ingredients are reported to function in cosmetics as skin protectants or skin conditioning agents. Several of the species reviewed in this report are used in foods (e.g., *Saccharomyces cerevisiae* is GRAS as a flavoring agent and adjuvant at a level not to exceed 5% in food [21CFR184.1983]).

According to 2023 VCRP survey data, Yeast Extract is reported to be used in 398 formulations (343 leave-on formulations and 55 rinse-off formulations). All other in-use ingredients are reported to be used in 81 formulations or less. The results of a concentration of use survey conducted by the Council indicate Galactomyces Ferment Filtrate has the highest concentration of use in a leave on formulation; it is used at up to 90.7% in moisturizing products. Based on VCRP data and concentration of use survey results, 18 of the yeast-derived ingredients are reported to be in use, and 38 are not.

Several in vitro dermal absorption assays were performed using 30% emulsions of Metschnikowia Agaves Extract, Pichia Anomala Extract, Pichia Heedii Extract, Pichia Minuta Extract, a Yeast Extract derived from *Candida saitoana*, and a Yeast Extract derived from *Metschnikowia reukaufii*. Dermal absorption in these studies ranged from 0.2 to 4.6% of the applied dose 24 h after application.

Median lethal doses (LD_{50}s) of > 2000 mg/kg were predicted in 3T3 neutral red uptake assays performed using Pichia Minuta Extract and Yeast Extract (derived from *Pichia naganishii*). An LD_{50} of > 2000 mg/kg was established in rats in acute dermal toxicity assays using 49.5% *Saccharomyces cerevisiae* cell wall (in HSCAS) and a *Saccharomyces cerevisiae* extract (in water). Similarly, no toxicity was observed in acute oral toxicity assays performed in mice using a *Galactomyces* ferment filtrate (up to 60000 mg/kg) or in rats with a yeast hydrolysate obtained from *Saccharomyces cerevisiae* (5000 mg/kg bw), 49.5% *Saccharomyces cerevisiae* cell wall (2000 mg/kg bw), a fermentate powder derived from *Saccharomyces cerevisiae* (2000 mg/kg), or *Candida oleophila* strain O (2.3-3.8 x 10^8 CFU). Acute inhalation toxicity was evaluated in rats using 49.5% *Saccharomyces cerevisiae* cell wall (2.09 mg/l). The median lethal concentration (LC_{50}) was determined to be > 2.09 mg/l. *Candida oleophila* strain O (1.2-5.2 x 10^8 CFU (in inhalation study); 1.1-2.0 x 10^7 CFU (in parenteral study)) was considered to be non-toxic in acute inhalation and acute parenteral assays performed in rats. No adverse effects were observed in an acute toxicity assay performed in mice inoculated with live *Pichia pastoris* cells (in saline; 1×10^6 CFU).

No significant adverse effects were noted in a 14-d assay in which rats were orally administered 1000 mg/kg bw/d yeast hydrolysate derived from *Saccharomyces cerevisiae*. In a different 14-d study, *Kluyveromyces marxianus* extracts (strains A4 and A5; 1.0 x 10^6 CFU/ml or 1.0 x 10^8 CFU/ml; in sterilized saline) were orally administered to female mice. Statistically significant lower spleen to body ratios and liver to body ratios were noted in mice treated with the high concentration of the A5 strain, and the low concentration of the A4 strain, respectively. *Phaffia rhodozyma* extract (up to 1000 mg/kg) in corn oil was given to rats, via gavage, for 28 d. The NOAEL was determined to be > 1000 mg/kg. Fermentate powder derived from *Saccharomyces cerevisiae* (in methylcellulose and water) was given to rats (20/sex/group) in a 90-d oral toxicity study (rats given up to 1500 mg/kg bw/d), and a 1-yr oral toxicity study (rats given up to 800 mg/kg bw/d). The NOAELs for the 90-d and 1-yr study were determined to be 1500 mg/kg bw/d and 800 mg/kg bw/d, respectively.

No mutagenicity was observed in in vitro genotoxicity studies performed on several yeast-derived ingredients (*Galactomyces* ferment filtrate, 90% yeast (*Saccharomyces cerevisiae*) cell wall, *Phaffia rhodozyma* extract, a trade name mixture containing 49% Phaffia Rhodozyma Extract, Pichia Minuta Extract, fermentate powder derived from *Saccharomyces cerevisiae*, trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, *Candida oleophila* strain O, Yeast Extract derived from *Pichia naganishii*. Similarly, negative results were also obtained in in vivo assays using a *Phaffia rhodozyma* extract, and 90% yeast (*Saccharomyces cerevisiae*) cell wall.

Treatment with *Saccharomyces cerevisiae* resulted in the growth inhibition or apoptosis of several cancer cell types in multiple anti-carcinogenicity assays. Cell lines that were inhibited by *Saccharomyces cerevisiae* include human metastatic breast cancer cells (MCF-7 and ZR-75-1), non-metastatic breast cancer cells (HCC70), squamous cell carcinoma of the tongue (SCC-4), adenocarcinomas of the colon (Caco-2, DLD1, and HCT116), and cervical cancer cells (HeLa).

The anti-inflammatory properties of a dried *Saccharomyces cerevisiae* fermentate was evaluated in 23 subjects. Inflammation was induced via histamine scratches in all subjects (saline used as control). Treatment with the fermentate resulted in faster and more effective inflammation reduction compared to the control.

The immunological cross-reactivity of several yeast species (including *Candida pseudotropicalis* (synonymous to *Kluyveromyces fragilis*), *Geotrichum candidum* (synonymous to *Galactomyces candidus*), and *Saccharomyces cerevisiae*) was evaluated in vitro. Significant cross-reactivity was only observed between *Candida* species. When skin prick tests were performed in 67 atopic patients using whole cell and disrupted cell extracts several yeast species including *Saccharomyces cerevisiae*, whole cell and disrupted cell extracts of *Saccharomyces cerevisiae* resulted in positive results in 41 and 31% of patients, respectively.

A delayed-type hypersensitivity test was performed in female mice using *Pichia pastoris* cells (in saline) on stratum corneum-removed skin. One control group was exposed to the same test substance on regular, intact, shaved skin, and another control group received saline only, on stratum corneum-removed skin. Seven days after administration, ear thickness was measured. Delayed type hypersensitivity was evaluated by inoculating ears with heat-killed *Pichia pastoris* cells. Results between control, vehicle-control, and *Pichia pastoris*-treated groups were similar.

Skin prick tests were performed in 47 individuals with an inhalant allergy to fungi; 10 non-allergic subjects were used as controls. Tests were performed using baker's yeast (*Saccharomyces cerevisiae*) extract and purified enolase obtained from baker's yeast. Clear reactions to the baker's yeast extract were noted in all fungi-allergic patients. Twenty-three patients showed a reaction to the baker's yeast enolase. No reactions were noted for either test substance in control subjects. Skin prick tests using a *Saccharomyces cerevisiae* extract were also performed in a different study, using 449 patients (226 with atopic dermatitis, 50 with allergic rhinitis and/or asthma, and 173 nonatopic controls). Ninety-two patients had positive skin prick tests to the extract. Patients with moderate to severe dermatitis displayed positive skin prick test reactions significantly more frequently than allergic rhinitis/asthma patients or nonatopic controls ($p < 0.001$). A significant correlation between total serum IgE and positive skin prick test results with *Saccharomyces cerevisiae* was seen ($r = 0.53$, $p < 0.001$).

Allergens of *Saccharomyces cerevisiae* were evaluated via an IgE-immunoblotting assay performed on 83 patients (70 atopic patients, 13 non-atopic controls). Forty-one atopic patients were positive in the IgE immunoblotting assay, revealing 22 IgE stained bands. Non-atopic serum and sera from atopic patients with negative skin prick tests to *Saccharomyces cerevisiae* were IgE negative in this experiment. In a similar assay, 20 patients (16 atopic, 4 non-atopic controls) were evaluated for IgE, IgA, and IgG responses to several common yeasts including *Saccharomyces cerevisiae*. Immunoblotting assays revealed IgE binding in all species (5 IgE binding bands in *Saccharomyces cerevisiae*). Prominent IgE binding was seen to a 46-kDa band of several species, including *Saccharomyces cerevisiae*. In addition, IgA and IgG responses were observed against *Saccharomyces cerevisiae*.

The cause of allergic alveolitis was evaluated in 12 Australian patients after a home evaluation for fungal growth. Twelve fungal species, including *Geotrichum candidum (*synonymous to *Galactomyces candidus*) was found in homes. When a precipitin test was performed on the subjects using freeze-dried fungal extracts and other allergens, 2 displayed positive reactions to *Geotrichum candidum* extract. Skin prick tests performed in the same patients resulted in one positive reaction to *Geotrichum candidum* extract. In an inhalation test performed in 6 of these patients, positive late responses were observed in 2 patients.

Normal human melanocytes treated with Galactomyces Ferment Filtrate (at concentrations of 20% or greater) exhibited a reduction in cell viability. Galactomyces Ferment Filtrate (5 and 10%) resulted in a reduction in melanin in human melanoma cells and normal human melanocytes. When the mechanism of action of Galactomyces Ferment Filtrate was evaluated, it was observed that 10% Galactomyces Ferment Filtrate increases the expression of Nrf2 and GST in human melanoma cells. The hyperpigmentation-reversal potential of Galactomyces Ferment Filtrate-containing skin care products was evaluated in 86 volunteers after a 1 yr treatment period. Treatment with Galactomyces Ferment Filtrate-containing products resulted in significant age-induced hyperpigmentation reversal.

The inhibitory effects of a *Saccharomyces cerevisiae* extract on melanogenesis were evaluated in B16F10 cells (melanocytes), alone, at doses of up to 200 µg/ml, and in melanocytes co-cultured with human keratinocytes, at doses of up to 500 µg/ml. Melanin synthesis decreased in a dose-dependent manner in melanocytes cultured with and without human keratinocytes. The inhibitory effect of *Saccharomyces cerevisiae* extract (up to 500 µg/ml) on tyrosinase was examined by a cell-free tyrosinase assay with mushroom tyrosinase, and by an intracellular tyrosinase assay in B16F10 cells. The test substance decreased the activity of intracellular tyrosinase in a dose-dependent manner, but had no direct inhibitory effect on tyrosinase itself.

Cellular viability analyses were performed using a trade name mixture containing 49% Phaffia Rhodozyma Extract and a trade name mixture containing 25% Saccharomyces Lysate Extract. Neither test substance was considered to be cytotoxic.

All in vitro dermal irritation assays yielded negative results (performed using a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall (tested neat), a trade name mixture containing 49% Phaffia Rhodozyma Extract (tested neat), powdered *Saccharomyces cerevisiae* extract (tested neat), three trade name mixtures containing up to 4.5% Saccharomyces Cerevisiae Extract (concentration tested unknown), a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate (tested neat), and two trade name mixtures containing 10% and 98% Saccharomyces Lysate Extract (both tested neat)). Slight irritation was observed in an irritation assay performed in rabbits using a mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall in 10% HSCAS (tested at 55% in water under semi-occlusive conditions). No

dermal irritation was observed in an assay performed in rabbits using a non-cosmetic product containing 57% *Candida oleophila* strain O. All test substances were considered to be non-irritating in dermal irritation assays performed in humans using a *Galactomyces* ferment filtrate (tested neat), a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall (tested neat), a cream consisting of 100% Lipomyces Lipid Bodies (tested neat), Metschnikowia Agaves Extract (15% in water), Pichia Anomala Extract (15% in water), Pichia Heedii Extract (15% in water), Pichia Minuta Extract (15% in water), a cosmetic formulation containing 1% *Saccharomyces cerevisiae* extract (tested neat), a Yeast Extract derived from *Candida mangoliae* (15% in water), a Yeast Extract derived from *Candida saitoana* (15% in water), a Yeast Extract derived from *Metschnikowia pulcherrima* (15% in water), and a Yeast Extract derived from *Metschnikowia reukaufii* (15% in water).

No sensitization potential was observed in several in chemico/in vitro sensitization assays. DPRAs (assess KE1 in the AOP) were performed using Phaffia Rhodozyma Extract (100 mM in acetonitrile) and trade name mixture containing 24% Saccharomyces Ferment Lysate Filtrate (100 mM acetonitrile). KeratinoSens™ assays (assess KE2 in the AOP) were performed using a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall, a trade name mixture containing 0.4% Hydrolyzed Yeast, a trade name mixture containing 49% Phaffia Rhodozyma Extract, Pichia Minuta Extract, a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, and Yeast Extracts derived from *Candida magnoliae*, *Metschnikowia reukaufii,* and *Pichia naganishii* (majority of test substances tested at up to 2000 µM). h-CLATs (assess KE3 in the AOP) were performed using Hydrolyzed Yeast (up to 5000 µg/ml) and Yeast Extract (derived from *Pichia naganishii* (concentration tested not stated)). A U-SENS™ (also assesses KE3 in the AOP) was performed using Pichia Minuta Extract (concentration tested not stated).

Several LLNAs (assess KE4 in the AOP) were performed in mice using *Saccharomyces cerevisiae* extract at concentrations of up to 50%. In one assay, the test substance was considered to be sensitizing at concentrations > 10%; however, in four other assays performed according to the same procedure, the test substance was considered to be non-sensitizing. No sensitization was observed in a GPMT of *Galactomyces* ferment filtrate (tested neat) or in a Buehler assay performed in guinea pigs using a mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall in 10% HSCAS (tested at 49.5% in water and carboxymethylcellulose).

Human studies were performed for several of the yeast-derived ingredients, all with negative results. HRIPTs of a skincare product containing 1.485% Galactomyces Ferment Filtrate (tested neat; n = 104), a facial treatment essence containing 92.675% Galactomyces Ferment Filtrate (tested neat; (n = 100)), a trade name mixture containing 0.4% Hydrolyzed Yeast (tested at 0.01%; final test concentration of Hydrolyzed Yeast: 0.00004%; n = 51), a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall (tested neat; n = 50), a cream containing 0.0135% Saccharomyces Ferment Lysate Filtrate (n = 52), a trade name mixture containing 2% Saccharomyces Ferment Lysate Filtrate (tested neat; n = 105), a cream containing 0.028% Saccharomyces Lysate Extract (tested neat; n = 50), and a trade name mixture containing 25% Saccharomyces Lysate Extract (tested at 10% in water; final test concentration of Saccharomyces Lysate Extract: 2.5%; n = 50); a lotion containing 0.0045% Yeast Extract (n = 52), 15% aq. Metschnikowia Agaves Extract (n = 112), Pichia Anomala Extract (n = 100 and n = 104), Pichia Heedii Extract (n = 106), Pichia Minuta Extract (n = 107), a Yeast Extract derived from *Candida saitoana* (n = 112), and a Yeast Extract derived from *Metschnikowia reukaufii* (n = 104) were negative for sensitization.

No phototoxicity was observed in EpiDerm™ assays performed using a trade name mixture containing 49% Phaffia Rhodozyma Extract and a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate (both test substances tested at up to 10%. Similarly, no phototoxicity or photosensitization was observed in assays performed on animals using *Galactomyces* ferment filtrate (nested neat).

All test substances were considered to be either minimally or non-irritating in in vitro ocular assays performed using a facial treatment essence containing 92.675% *Galactomyces* ferment filtrate, a trade name mixture containing 8-10% Hydrolyzed Saccharomyces Cell Wall, a trade name mixture containing 49% Phaffia Rhodozyma Extract, Pichia Minuta Extract, several trade name mixtures containing Saccharomyces Cerevisiae Extract (up to 20%), a trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate, two trade name mixtures containing Saccharomyces Lysate Extract (up to 98%), and Yeast Extract derived from *Pichia naganishii*. No irritation was observed in an ocular irritation assay performed in rabbits using *Galactomyces* ferment filtrate (tested neat). Minimal irritation was observed in an ocular irritation assay performed in rabbits using a mixture containing 90% *Saccharomyces cerevisiae* cell wall in 10% HSCAS and in an assay performed in rabbits using a non-cosmetic product containing 57% *Candida oleophila* strain O. Resolvable irritation was observed in rabbits treated with an undiluted powdered *Saccharomyces cerevisiae* extract.

Three out of 6 pilot-plant production workers not wearing personal protective equipment displayed respiratory reactions when working in a facility manufacturing a product containing *Candida oleophila* strain O (as an active ingredient at 57% by weight). A 29-yr-old woman suffered from multiple severe anaphylactic reactions following a meal of olive sauce, pasta, and feta cheese. Skin prick and serum immunologic E (IgE) tests revealed were positive to several molds including baker's yeast (*Saccharomyces cerevisiae*). A 33-yr-old woman with a history of allergies and asthma reported anaphylaxis episodes that were related to ingestion of beer, chips, olive, and wine. An immunoblotting assay revealed a high-intensity IgE-binding zone, when evaluating *Saccharomyces cerevisiae* extract, between 100 kDa and 29 kDa, and a band around 17 kDa. In a different case report, a 25-yr-old woman was admitted to the hospital with a dry cough, low-grade fever, and focal patchy

shadow of pulmonary infiltrates. Skin prick tests were positive to *Saccharomyces cerevisiae*. Bronchoprovocation testing performed 3 mo later using *Saccharomyces cerevisiae* antigens yielded positive results, and the patient exhibited a coughing attack, high fever, and ticklish throat within 15 min of exposure. Serum C-reactive protein and sputum eosinophils were increased on the day after provocation testing with *Saccharomyces cerevisiae* antigen. A 48-yr-old baker reported respiratory symptoms 1-2 h after the start of a workday. Skin prick tests were performed using extracts of wet and dry yeast (at dilutions of 10^{-4} – 10^{-2}), as well as other potential allergens. Positive responses to the wet and dry yeast extracts were observed at the 10^{-2} dilution. The patient was diagnosed with occupational asthma caused by *Saccharomyces cerevisiae* sensitization, and began to use conventional wet yeast without symptoms.

DISCUSSION

The 56 ingredients in this report are derived from various species of yeast, the majority of which are from the Saccharomycetes class. The Panel reviewed these yeast-derived ingredients and determined that the data are sufficient to conclude that 11 yeast-derived ingredients and 22 generic-named yeast-derived ingredients, when derived from species of yeast included in the report with both dermal sensitization and food use status, are safe in cosmetics in the present practices of use and concentration; the Panel also concluded that data were insufficient to determine the safety of the remaining 23 ingredients. Data profiles for these ingredients were considered sufficient when food use data (via published literature, GRAS status, and/or QPS status) and sensitization data were available for the ingredient itself, or for the species of yeast used to derive the ingredient. (The need for systemic toxicity data was mitigated for those ingredients that are used in foods, have a GRAS status, or QPS status because exposure via ingestion would be far greater than exposure via cosmetics.) Some of the yeast-derived ingredients reviewed herein are generic, and it is unknown which species, or how many species, are used to manufacture the ingredients (e.g., Yeast Extract). These generic ingredients were considered to be safe by the Panel if formulated using a species of yeast included in this report that had both food use and dermal sensitization data. These species include *Candida magnoliae*, *Candida saitoana*, *Metschnikowia agaves*, *Metschnikowia reukaufii*, *Pichia anomala*, *Pichia minuta*, *Phaffia rhodozyma*, *Saccharomyces cerevisiae*, and *Saccharomyces pastorianus*. Ingredients lacking some or all of the data components described herein were considered to have insufficient safety data, and depending on which data are lacking, systemic toxicity data (via 28-d dermal toxicity assay), sensitization data, or both, are required (food use/GRAS status/QPS status may be used in lieu of systemic toxicity data). It should be noted that if 28-d dermal toxicity data are provided and these data indicate absorption of the ingredient, other toxicity endpoints would be required to determine safety (e.g., developmental and reproductive toxicity).

The Panel noted that elevated levels of heavy metals and pesticide residues may be present in these yeast-derived ingredients and stressed that the cosmetics industry should continue to use the necessary procedures to minimize impurities in cosmetic formulations according to limits set by the FDA and EPA. In addition, the Panel noted that volatile compounds (e.g., benzaldehyde, hexane) may be present in yeast-derived ingredients. However, these compounds are expected to become volatilized prior to the preparation of the final cosmetic product containing these ingredients, and thus would be present in none to minimal amounts.

The Panel also noted incidences of IgE-mediated hypersensitivity following inhalation exposure to certain yeast species (e.g., *Saccharomyces cerevisiae*). However, these reactions were observed in subjects exposed to live yeasts at high concentrations. Yeasts in cosmetic ingredients are lysed and inactivated, and are reported to be used in inhalable cosmetic products at very low concentrations (≤ 1.1%). In addition, safety of these ingredients was supported by the minimal amount of hypersensitivity case reports present in the literature, in comparison to the widespread historical use and consumption of various species of yeast.

The Panel discussed the issue of incidental inhalation exposure that could result with the use of some of these ingredients in cosmetics (e.g., Galactomyces Ferment Filtrate is reported to be used at 1.1% in face powders). Inhalation toxicity data were limited; however, the Panel noted that in aerosol products, the majority of droplets/particles would not be respirable to any appreciable amount. Furthermore, droplets/particles deposited in the nasopharyngeal or tracheobronchial regions of the respiratory tract present no toxicological concerns based on the chemical and biological properties of these ingredients. Coupled with the small actual exposure in the breathing zone and the low concentrations at which the ingredients are used in potentially inhaled products, the available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local respiratory or systemic effects. A detailed discussion and summary of the Panel's approach to evaluating incidental inhalation exposures to ingredients in cosmetic products is available at https://www.cir-safety.org/cir-findings.

The Panel's respiratory exposure resource document (see link above) notes that airbrush technology presents a potential safety concern, and that no data are available for consumer habits and practices thereof. As a result of deficiencies in these critical data needs, the safety of cosmetic ingredients applied by airbrush delivery systems cannot be determined by the Panel. Therefore, the Panel has concluded the data are insufficient to support the safe use of cosmetic ingredients applied via an airbrush delivery system.

CONCLUSION

The Expert Panel for Cosmetic Ingredient Safety concluded that the following 11 of the 56 yeast-derived ingredients are safe in cosmetics in the present practices of use and concentration described in this safety assessment.

Hydrolyzed Candida Saitoana Extract
Galactomyces Ferment Filtrate
Hydrolyzed Metschnikowia Agaves Extract*
Metschnikowia Agaves Extract*
Hydrolyzed Metschnikowia Reukaufii Extract*
Metschnikowia Reukaufii Lysate Extract*
Phaffia Rhodozyma Extract*
Phaffia Rhodozyma Ferment Extract*
Pichia Anomala Extract
Pichia Minuta Extract*
Saccharomyces Cerevisiae Extract

In addition, the Panel concluded that the following 22 generic-named yeast-derived ingredients (ingredients in which the species of yeast used in manufacturing was not provided in the *Dictionary*), when derived from species of yeast included in the report, are safe in cosmetics in the present practices of use and concentration described in this safety assessment:

Hydrolyzed Saccharomyces Cell Wall*
Hydrolyzed Saccharomyces Extract*
Hydrolyzed Saccharomyces Lysate Extract*
Hydrolyzed Yeast
Hydrolyzed Yeast Extract
Lactic Yeasts*
Pichia Extract*
Saccharomyces*
Saccharomyces Extract*
Saccharomyces Ferment
Saccharomyces Ferment Extract*
Saccharomyces Ferment Extract Lysate Filtrate
Saccharomyces Ferment Filtrate
Saccharomyces Ferment Lysate Extract*
Saccharomyces Ferment Lysate Filtrate
Saccharomyces Lysate
Saccharomyces Lysate Extract
Saccharomyces Lysate Extract Filtrate*
Saccharomyces Lysate Filtrate*
Yeast
Yeast Extract
Yeast Ferment Extract

The Panel also concluded that the available data are insufficient to make a determination of safety for the remaining 23 ingredients under the intended conditions of use in cosmetic formulations.

Hydrolyzed Candida Bombicola Extract**
Hydrolyzed Kluyveromyces Extract**
Hydrolyzed Metschnikowia Shanxiensis**
Hydrolyzed Torulaspora Delbrueckii Extract**
Kluyveromyces Extract
Lipomyces Lipid Bodies**
Lipomyces Oil**
Lipomyces Oil Extract**
Metschnikowia Henanensis Extract**
Metschnikowia Viticola Extract**
Pichia Caribbica Ferment**
Pichia Ferment Extract Filtrate**
Pichia Ferment Lysate Filtrate
Pichia Heedii Extract**
Pichia Pastoris Ferment Filtrate**
Schizosaccharomyces Ferment Extract Filtrate**
Schizosaccharomyces Ferment Filtrate
Schizosaccharomyces Pombe Extract**
Torulaspora Delbrueckii Extract**
Torulaspora Delbrueckii Ferment**
Yarrowia Lipolytica Extract**
Yarrowia Lipolytica Ferment Lysate**
Yarrowia Lipolytica Oil**

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

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

TABLES

Table 1. INCI names, definitions, and reported functions of the yeast-derived ingredients in this safety assessment[1]

Ingredient (CAS No.)	Definition	Function
Galactomyces Ferment Filtrate	Galactomyces Ferment Filtrate is a filtrate of the product obtained by the fermentation of a growth media by the microorganism, *Galactomyces candidus*, *Galactomyces fermentans*, or *Galactomyces reessii*.	Skin-Conditioning agents - Humectant
Hydrolyzed Candida Bombicola Extract	Hydrolyzed Candida Bombicola Extract is the hydrolysate of an extract of *Candida bombicola* obtained by acid, enzyme or other method of hydrolysis.	Surfactants – Cleansing Agents
Hydrolyzed Candida Saitoana Extract	Hydrolyzed Candida Saitoana Extract is the hydrolysate of an extract of *Candida saitoana* derived by acid, enzyme or other method of hydrolysis.	Skin Protectants
Hydrolyzed Kluyveromyces Extract	Hydrolyzed Kluyveromyces Extract is the hydrolysate of Kluyveromyces Extract derived by acid, enzyme or other method of hydrolysis.	Skin-Conditioning Agents - Miscellaneous
Hydrolyzed Metschnikowia Agaves Extract [1309127-75-0]	Hydrolyzed Metschnikowia Agaves Extract is the hydrolysate of an extract of the yeast, *Metschnikowia agaves* derived by acid, enzyme or other method of hydrolysis.	Skin Protectants
Hydrolyzed Metschnikowia Reukaufii Extract	Hydrolyzed Metschnikowia Reukaufii Extract is the extract of the hydrolysate of Metschnikowia Reukaufii Lysate Extract derived by acid, enzyme or other method of hydrolysis.	Skin Protectants
Hydrolyzed Metschnikowia Shanxiensis Extract	Hydrolyzed Metschnikowia Shanxiensis Extract is the hydrolysate of an extract of the microorganism, *Metschnikowia shanxiensis.*	Skin Protectants
Hydrolyzed Saccharomyces Cell Wall	Hydrolyzed Saccharomyces Cell Wall is the hydrolysate of the cell walls of *Saccharomyces* derived by acid, enzyme or other method of hydrolysis.	Film Formers Hair Conditioning Agents Skin-Conditioning Agents - Humectant Slip Modifiers
Hydrolyzed Saccharomyces Extract	Hydrolyzed Saccharomyces Extract is the hydrolysate of an extract of Saccharomyces derived by acid, enzyme or other method of hydrolysis.	Skin-Conditioning Agents - Emollient
Hydrolyzed Saccharomyces Lysate Extract	Hydrolyzed Saccharomyces Lysate Extract is the extract of the product obtained by the hydrolysis of Saccharomyces Lysate Extract.	Skin-Conditioning Agents - Humectant
Hydrolyzed Torulaspora Delbrueckii Extract	Hydrolyzed Torulaspora Delbrueckii Extract is the hydrolysate of an extract of *Torulaspora delbrueckii* derived by acid, enzyme or other method of hydrolysis.	Skin Protectants
Hydrolyzed Yeast	Hydrolyzed Yeast is the hydrolysate of yeast derived by acid, enzyme or other method of hydrolysis.	Hair-Conditioning Agents; Skin-Conditioning Agents - Miscellaneous
Hydrolyzed Yeast Extract	Hydrolyzed Yeast Extract is the hydrolysate of Yeast Extract derived by acid, enzyme or other method of hydrolysis.	Skin-Conditioning Agents - Miscellaneous
Kluyveromyces Extract	Kluyveromyces Extract is the extract of *Kluyveromyces lactis* or *Kluyveromyces fragilis*.	Skin-Conditioning Agents - Humectant
Lactic Yeasts [68876-77-7]	Lactic Yeasts is a Yeast obtained from milk.	Not Reported
Lipomyces Lipid Bodies	Lipomyces Lipid Bodies are the lipid-rich organelles produced through fermentation by *Lipomyces*.	Skin-Conditioning Agents - Emollient
Lipomyces Oil	Lipomyces Oil is the oil produced through fermentation by the fungus, *Lipomyces starkeyi*.	Hair-Conditioning Agents; Skin-Conditioning Agents – Humectant; Surfactants-Cleansing Agents; Surfactants-Emulsifying Agents
Lipomyces Oil Extract	Lipomyces Oil Extract is the extract of Lipomyces Oil	Skin-Conditioning Agents - Emollient
Metschnikowia Agaves Extract	Metschnikowia Agaves Extract is the extract of the yeast, *Metschnikowia agaves*.	Skin Protectants
Metschnikowia Henanesis Extract	Metschnikowia Henanensis Extract is the extract of the fungus, *Metschnikowia henanensis.*	Skin-Conditioning Agents - Humectants
Metschnikowia Reukaufii Lysate Extract	Metschnikowia Reukaufii Lysate Extract is the extract of a lysate of the cultured cells of *Metschnikowia reukaufii.*	Skin Protectants
Metschnikowia Viticola Extract	Metschnikowia Viticola Extract is the extract of the yeast, *Metschnikowia viticola.*	Skin-Conditioning Agents - Humectant
Pichia Caribbica Ferment	Pichia Caribbica Ferment is the product obtained by the fermentation of *Pichia caribbica*.	Skin-Conditioning Agents - Humectant
Pichia Extract	Pichia Extract is the extract of various species of the microorganism, *Pichia.*	Skin Protectants
Pichia Ferment Extract Filtrate	Pichia Ferment Extract Filtrate is a filtrate of an extract of the product obtained through fermentation by the microorganism, *Pichia pastoris.*	Skin Protectants; Skin-Conditioning Agents – Emollient; Skin-Conditioning Agents - Humectant
Pichia Ferment Lysate Filtrate	Pichia Ferment Lysate Filtrate is a filtrate of a lysate of the product obtained by the fermentation of *Pichia pastoris*, *Pichia populi* or *Pichia stipitis.*	Humectants; Skin Protectants; Skin-Conditioning Agents – Miscellaneous

Table 1. INCI names, definitions, and reported functions of the yeast-derived ingredients in this safety assessment[1]

Ingredient (CAS No.)	Definition	Function
Pichia Pastoris Ferment Filtrate	Pichia Pastoris Ferment Filtrate is a filtrate of the product obtained by the fermentation of a growth media by the microorganism, *Pichia pastoris*.	Skin-Conditioning Agents – Miscellaneous
Phaffia Rhodozyma Extract	Phaffia Rhodozyma Extract is the extract of the microorganism, *Phaffia rhodozyma*.	Hair-Conditioning Agents; Skin-Conditioning Agents - Miscellaneous
Phaffia Rhodozyma Ferment Extract	Phaffia Rhodozyma Ferment Extract is the extract of the fermentation product of *Phaffia rhodozyma*.	Antioxidants; Colorants; Skin-Conditioning Agents - Emollient
Pichia Anomala Extract [1033319-29-7]	Pichia Anomala Extract is the extract of the yeast, *Pichia anomala*.	Skin Protectants
Pichia Heedii Extract [1801269-82-8]	Pichia Heedii Extract is the extract of the yeast, *Pichia heedii*.	Skin Protectants
Pichia Minuta Extract [2009239-94-3]	Pichia Minuta Extract is the extract of the microorganism, *Pichia minuta.*	Skin Protectants
Saccharomyces	Saccharomyces is one or more species of the microorganism, *Saccharomyces*	Anti-Acne Agents; Anti-Microbial Agents; Binders; Skin Protectants
Saccharomyces Cerevisiae Extract [84604-16-0]	Saccharomyces Cerevisiae Extract is the extract of the yeast cells of *Saccharomyces cerevisiae*.	
Saccharomyces Extract	Saccharomyces Extract is the extract of Saccharomyces	Antioxidants; Hair-Conditioning Agents; Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Saccharomyces Ferment	Saccharomyces Ferment is the product obtained through fermentation by the microorganism, *Saccharomyces*.	Not Reported
Saccharomyces Ferment Extract	Saccharomyces Ferment Extract is the extract of the product obtained by the fermentation of media by *Saccharomyces*.	Flavoring Agents Fragrance Ingredients
Saccharomyces Ferment Extract Lysate Filtrate	Saccharomyces Ferment Extract Lysate Filtrate is the filtrate of the product obtained after the lysis of the cultured cells of the microorganism, *Saccharomyces*.	Skin Protectants
Saccharomyces Ferment Filtrate	Saccharomyces Ferment Filtrate is a filtrate of the product obtained by the fermentation of a growth media by the microorganism, *Saccharomyces*.	Skin-Conditioning Agents - Humectant
Saccharomyces Ferment Lysate Extract	Saccharomyces Ferment Lysate Extract is the extract of the lysed cells of *Saccharomyces* grown in culture.	Skin Protectants
Saccharomyces Ferment Lysate Filtrate	Saccharomyces Ferment Lysate Filtrate is the filtrate of a lysate of the product obtained by the fermentation of *Saccharomyces*.	Skin Protectants
Saccharomyces Lysate [8013-01-2]	Saccharomyces Lysate is a lysate of the product obtained by the fermentation of *Saccharomyces*.	Not Reported
Saccharomyces Lysate Extract [8013-01-2]	Saccharomyces Lysate Extract is the extract of Saccharomyces Lysate	Skin-Conditioning Agents – Humectant; Skin-Conditioning Agents - Miscellaneous
Saccharomyces Lysate Extract Filtrate	Saccharomyces Lysate Extract Filtrate is a filtrate of the extract of the product obtained by the lysis of *Saccharomyces* cells.	Skin-Conditioning Agents - Miscellaneous
Saccharomyces Lysate Filtrate	Saccharomyces Lysate Filtrate is a filtrate of lysed *Saccharomyces* grown in culture.	Hair-Conditioning Agents; Skin Protectants
Schizosaccharomyces Ferment Extract Filtrate	Schizosaccharomyces Ferment Extract Filtrate is a filtrate of an extract obtained by the fermentation of *Schizosaccharomyces*.	Humectants; Skin-Conditioning Agents - Miscellaneous
Schizosaccharomyces Ferment Filtrate	Schizosaccharomyces Ferment Filtrate is a filtrate of the product obtained by the fermentation of a growth media by the microorganism, *Schizosaccharomyces*.	Hair-Conditioning Agents; Humectants; Skin-Conditioning Agents – Miscellaneous
Schizosaccharomyces Pombe Extract	Schizosaccharomyces Pombe Extract is the extract of the yeast, *Schizosaccharomyces pombe*.	Skin-Conditioning Agents – Miscellaneous
Torulaspora Delbrueckii Extract [1291071-26-5]	Torulaspora Delbrueckii Extract is the extract of the yeast, *Torulaspora delbrueckii*.	Skin Protectants
Torulaspora Delbrueckii Ferment [1291071-26-5]	Torulaspora Delbrueckii Ferment is the product obtained by the fermentation of *Torulaspora delbrueckii*.	Skin-Conditioning Agents - Miscellaneous
Yarrowia Lipolytica Extract	Yarrowia Lipolytica Extract is the extract of the microorganism, *Yarrowia lipolytica* obtained through fermentation.	Skin-Conditioning Agents - Humectant
Yarrowia Lipolytica Ferment Lysate	Yarrowia Lipolytica Ferment Lysate is the product obtained after the lysis of the cultured cells of the microorganism, *Yarrowia lipolytica.*	Skin-Conditioning Agent – Humectant
Yarrowia Lipolytica Oil	Yarrowia Lipolytica Oil is the oil derived from the fermentation of the fungus, *Yarrowia lipolytica* grown in culture.	Skin-Conditioning Agent - Emollient
Yeast [68876-77-7]	Yeast is a class of microorganisms (Saccharomycetes) characterized by their lack of photosynthetic ability, existence as unicellular or simple irregular filaments, and reproduction by budding or direct division.	Not Reported
Yeast Extract [68876-77-7; 8013-01-2]	Yeast Extract is the extract of Yeast.	Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Yeast Ferment Extract	Yeast Ferment Extract is the extract of the product obtained by the fermentation of *Saccharomyces cerevisiae*.	Skin-Conditioning Agents – Miscellaneous

Table 2. Chemical properties of yeast-derived cosmetic ingredients

Property	Value	Reference
Saccharomyces Cerevisiae Extract		
Physical Form	liquid	[10]
Color	clear-yellow	[10]
Odor	faint	[10]
Specific Gravity (@ 20ºC)	1.035 – 1.055	[10]
Vapor pressure (mmHg @ 105ºC)	3.83	[2]
Refraction Index (RIU (@ 20°C))	1.035 – 1.055	[10]
Yeast		
Physical Form	powder, granules, or flakes	[9]
Color	light brown - buff	[9]
Yeast Extract*		
Physical Form	liquid	[19]
Color	clear-pale yellow	[19]
Odor	characteristic	[19]
Water Solubility	soluble	[19]
Specific Gravity (@ 25ºC)	1.05 – 1.15	[19]
Refraction Index (RIU (@ 25°C))	1.3920 – 1.5000	[19]

*derived from *Saccharomyces cerevisiae*

Table 3. Taxonomy of yeast-derived ingredients[1,120]

INCI Ingredient	Class	Order	Family	Genus	Associated Genus and Species/Synonyms	Synonyms**
Galactomyces Ferment Filtrate*	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Geotrichum*	*Galactomyces candidus*	*Dipodascus geotrichum* *Endomyces geotrichum* *Galactomyces geotrichum* *Geotrichum candidum*
	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Dipoascus*	*Galactomyces fermentans*	-
	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Galactomyces*	*Galactomyces reessii*	*Endomyces reessii* *Dipodascus reessii*
Hydrolyzed Candida Bombicola Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetales*	*Starmerella*	*Candida bombicola*	*Starmerella bombicola*
Hydrolyzed Candida Saitoana Extract	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Candida*	*Candida saitoana*	-
Hydrolyzed Kluyveromyces Extract*	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Kluyveromyces*	*Kluyveromyces fragilis*	*Candida kefyr* *Candida pseudotropicalis* *Dekkeromyces marxianus* *Guilliermondella marxiana* *Kluyveromyces cicerisporus* *Kluyveromyces marxianus* *Saccharomyces marxianus* *Zygofabospora marxiana* *Zygorenospora marxiana* *Zygosaccharomyces marxianus*
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Kluyveromyces*	*Kluyveromyces lactis*	*Torulaspora lactis* *Saccharomyces lactis* *Kluyveromyces drosophilarum* *Candida sphaerica*
Hydrolyzed Metschnikowia Agaves Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia agaves*	-
Hydrolyzed Metschnikowia Reukaufii Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia reukaufii*	*Candida reukaufii*
Hydrolyzed Metschnikowia Shanxiensis	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia shanxiensis*	-
Hydrolyzed Saccharomyces Cell Wall	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	*Saccharomyces bayanus*	*Saccharomyces abulensis*
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	*Saccharomyces cerevisiae*	*Mycoderma cerevisiae* *Candida robusta* *Saccharomyces capensis* *Saccharomyces italicus* *Saccharomyces oviformis* *Saccharomyces uvarum var. melibiosus*
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	*Saccharomyces pastorianus*	*Saccharomyces carlsbergensis* *Saccharomyces monacensis*
Hydrolyzed Saccharomyces Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Hydrolyzed Saccharomyces Lysate Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-

Table 3. Taxonomy of yeast-derived ingredients[1,120]

INCI Ingredient	Class	Order	Family	Genus	Associated Genus and Species/Synonyms	Synonyms**
Hydrolyzed Torulaspora Delbrueckii Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Torulaspora*	*Torulaspora delbrueckii*	*Saccharomyces delbrueckii* *Saccharomyces fermentati* *Saccharomyces rosei* *Candida colliculosa*
Hydrolyzed Yeast	Saccharomycetes	-	-	-	-	-
Hydrolyzed Yeast Extract	Saccharomycetes	-	-	-	-	-
Kluyveromyces Extract*	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Kluyveromyces*	*Kluyveromyces fragilis*	*Candida kefyr* *Candida pseudotropicalis* *Dekkeromyces marxianus* *Guilliermondella marxiana* *Kluyveromyces cicerisporus* *Kluyveromyces marxianus* *Saccharomyces marxianus* *Zygofabospora marxiana* *Zygorenospora marxiana* *Zygosaccharomyces marxianus*
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Kluyveromyces*	*Kluyveromyces lactis*	*Torulaspora lactis* *Saccharomyces lactis* *Kluyveromyces drosophilarum* *Candida sphaerica*
Lactic Yeasts	Saccharomycetes	-	-	-	-	-
Lipomyces Lipid Bodies	Saccharomycetes	Saccharomycetales	*Lipomycetaceae*	*Lipomyces*	*Lipomyces sp.*	-
Lipomyces Oil	Saccharomycetes	Saccharomycetales	*Lipomycetaceae*	*Lipomyces*	*Lipomyces starkeyi*	-
Lipomyces Oil Extract	Saccharomycetes	Saccharomycetales	*Lipomycetaceae*	*Lipomyces*	*Lipomyces starkeyi*	-
Metschnikowia Agaves Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia agaves*	-
Metschnikowia Henanensis Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia henanensis*	-
Metschnikowia Reukaufii Lysate Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia reukaufii*	*Candida reukaufii*
Metschnikowia Viticola Extract	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia viticola*	-
Pichia Anomala Extract	Saccharomycetes	Saccharomycetales	*Phaffomycetaceae*	*Wickerhamomyces*	*Pichia anomala*	*Whickerhamomyces anomalus* *Saccharomyces anomalus* *Endomyces anomalus* *Hansenula anomala* *Pichia anomalus* *Willia anomala*
Pichia Caribbica Ferment	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Meyerozyma*	*Pichia caribbica*	*Meyerozyma caribbica* *Candida fermentati* *Torula fermentati*
Pichia Extract	Saccharomycetes	Saccharomycetales	*Pichiaceae*	-	-	-
Pichia Ferment Extract Filtrate	Saccharomycetes	Saccharomycetales	*Phaffomycetaceae*	*Komagatella*	*Pichia pastoris*	*Komagataella pastoris* *Zygosaccharomyces pastoris*
Pichia Ferment Lysate Filtrate*	Saccharomycetes	Saccharomycetales	*Phaffomycetaceae*	*Barnettozyma*	*Pichia populi*	*Barnettozyma populi* *Hansenula populi*
Pichia Ferment Lysate Filtrate*	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Scheffersomyces*	*Pichia stipitis*	*Scheffersomyces stipitis* *Yamadazyma stipitis*
Pichia Heedii Extract	Saccharomycetes	Saccharomycetales	*Pichiaceae*	*Pichia*	*Pichia heedii*	-

Table 3. Taxonomy of yeast-derived ingredients[1,120]

INCI Ingredient	Class	Order	Family	Genus	Associated Genus and Species/Synonyms	Synonyms**
Pichia Minuta Extract	Saccharomycetes	Saccharomycetales	*Pichiaceae*	*Ogataea*	*Pichia minuta*	*Ogataea minuta* *Hansenula minuta* *Candida methanolovescens* *Torulopsis methanolovescens*
Pichia Pastoris Ferment Filtrate	Saccharomycetes	Saccharomycetales	*Phaffomycetaceae*	*Komagatella*	*Pichia pastoris*	*Komagataella pastoris* *Zygosaccharomyces pastoris*
Phaffia Rhodozyma Extract	Tremellomycetes	Cystofilobasidales	*Mrakiaceae*	*Phaffia*	*Phaffia rhodozyma*	*Cryptococcus rhodozymus* *Rhodomyces dendrorhous* *Xanthophyllomyces dendrorhous*
Phaffia Rhodozyma Ferment Extract	Tremellomycetes	Cystofilobasidales	*Mrakiaceae*	*Phaffia*	*Phaffia rhodozyma*	*Cryptococcus rhodozymus* *Rhodomyces dendrorhous* *Xanthophyllomyces dendrorhous*
Saccharomyces	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Cerevisiae Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	*Saccharomyces cerevisiae*	*Mycoderma cerevisiae* *Candida robusta* *Saccharomyces capensis* *Saccharomyces italicus* *Saccharomyces oviformis* *Saccharomyces uvarum var. melibiosus*
Saccharomyces Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment Extract Lysate Filtrate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment Filtrate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment Lysate Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Ferment Lysate Filtrate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Lysate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Lysate Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Lysate Extract Filtrate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Saccharomyces Lysate Filtrate	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	-	-
Schizosaccharomyces Ferment Extract Filtrate	Schizosaccharomycetes	Schizosaccharomycetales	*Schizosaccharomycetaceae*	*Schizosaccharomyces*	-	-
Schizosaccharomyces Ferment Filtrate	Schizosaccharomycetes	Schizosaccharomycetales	*Schizosaccharomycetaceae*	*Schizosaccharomyces*	-	-
Schizosaccharomyces Pombe Extract	Schizosaccharomycetes	Schizosaccharomycetales	*Schizosaccharomycetaceae*	*Schizosaccharomyces*	*Schizosaccharomyces pombe*	*Schizosaccharomyces malidevorans*
Torulaspora Delbrueckii Extract	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Torulaspora*	*Torulapora delbrueckii*	*Saccharomyces delbrueckii* *Saccharomyces fermentati* *Saccharomyces rosei* *Candida colliculosa*

Table 3. Taxonomy of yeast-derived ingredients[1,120]

INCI Ingredient	Class	Order	Family	Genus	Associated Genus and Species/Synonyms	Synonyms**
Torulaspora Delbrueckii Ferment	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Torulaspora*	*Torulapora delbrueckii*	*Saccharomyces delbrueckii* *Saccharomyces fermentati* *Saccharomyces rosei* *Candida colliculosa*
Yarrowia Lipolytica Extract	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Yarrowia*	*Yarrowia lipolytica*	*Endomycopsis lipolytica* *Mycotorula lipolytica* *Candida lipolytica*
Yarrowia Lipolytica Ferment Lysate	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Yarrowia*	*Yarrowia lipolytica*	*Endomycopsis lipolytica* *Mycotorula lipolytica* *Candida lipolytica*
Yarrowia Lipolytica Oil	Saccharomycetes	Saccharomycetales	*Dipodascaceae*	*Yarrowia*	*Yarrowia lipolytica*	*Endomycopsis lipolytica* *Mycotorula lipolytica* *Candida lipolytica*
Yeast	Saccharomycetes	-	-	-	-	-
Yeast Extract***	Saccharomycetes	-	-	-	-	-
	Saccharomycetes	Saccharomycetales	*NR*	*Starmerella*	*Candida magnoliae*	*Starmerella magnoliae* *Torulopsis magnoliae*
	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Kurtzmaniella*	*Candida oleophila*	-
	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Candida*	*Candida saitoana*	-
	Saccharomycetes	Saccharomycetales	*Debaryomycetaceae*	*Debaryomyces*	*Debaryomyces nepalensis*	-
	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia agaves*	-
	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia reukaufii*	*Candida reukaufii*
	Saccharomycetes	Saccharomycetales	*Metschnikowiaceae*	*Metschnikowia*	*Metschnikowia pulcherrima*	*Candida pulcherrima*
	Saccharomycetes	Saccharomycetales	*Phaffomycetaceae*	*Wickerhamomyces*	*Pichia anomala*	*Whickerhamomyces anomalus* *Saccharomyces anomalus* *Endomyces anomalus* *Hansenula anomala* *Pichia anomalus* *Willia anomala*
	Saccharomycetes	Saccharomycetales	*Pichiaceae*	*Pichia*	*Pichia heedii*	-
	Saccharomycetes	Saccharomycetales	*Pichiaceae*	*Ogataea*	*Pichia minuta*	*Ogataea minuta* *Hansenula minuta* *Candida methanolovescens* *Torulopsis methanolovescens*
	Saccharomycetes	Saccharomycetales	*Pichiaceae*	*Ogataea*	*Pichia naganishii*	*Ogataea naganishii*
	Saccharomycetes	Saccharomycetales	*Saccharomycetaceae*	*Saccharomyces*	*Saccharomyces cerevisiae*	*Mycoderma cerevisiae* *Candida robusta* *Saccharomyces capensis* *Saccharomyces italicus* *Saccharomyces oviformis* *Saccharomyces uvarum var. melibiosus*
Yeast Ferment Extract	Saccharomycetes	-	-	-	-	-

*ingredient has more than one associated genus and species according to the *Dictionary*, and therefore has multiple entries in this table

**synonyms include heterotypic synonyms, homotypic synonyms, and basionyms

***although this is a generic yeast ingredient, several species have been identified in unpublished literature[19,20] that correspond to "Yeast Extract"; it is unknown whether or not these species are the only species used in the formulation of Yeast Extract

NR = not reported

Table 4. Fatty acid composition of several yeast species (measured as % of total fatty acids)[21]

Fatty acid	*Candida kefyr* (synonymous to *Kluyveromyces fragilis*)	*Candida lipolytica* (synonymous to *Yarrowia lipolytica*)	*Saccharomyces cerevisiae*
decanoic (C10:0)	0.06 ± 0.01	-	6.15 ± 1.18
lauric (C12:0)	0.22 ± 0.02	-	7.59 ± 1.35
myristic (C14:0)	2.05 ± 0.13	-	1.90 ± 0.05
myristoleic (C14:1)	0.24 ± 0.05	-	0.98 ± 0.04
pentadecanoic (C15:0)	0.25 ± 0.06	0.87 ± 0.11	-
palmitic (C16:0)	20.06 ± 1.55	11.99 ± 2.23	12.72 ± 1.45
palmitoleic (C16:1)	27.46 ± 2.48	17.22 ± 1.12	51.21 ± 2.25
heptadecanoic (C17:1)	0.08 ± 0.01	2.71 ± 0.43	-
stearic (C18:0)	1.15 ± 0.04	0.77 ± 0.02	0.95 ± 0.02
cis-9-octadecanoic (C18:1(9))	24.61 ± 2.38	42.85 ± 3.65	18.50 ± 1.33
cis-11-octadecanoic (C18:1(11))	0.40 ± 0.02	0.58 ± 0.04	-
linoleic (C18:2)	19.41 ± 2.13	23.01 ± 2.15	-
linolenic (C18:3)	4.01 ± 0.66	-	-

Table 5. Nutrient, amino acid, and mineral composition of *Saccharomyces cerevisiae* and *Yarrowia lipolytica*[121]

Nutrient (%)	*Yarrowia lipolytica*	*Saccharomyces cerevisiae*
crude protein	45.5	40.34
crude fat	1.47	0.51
dry matter	97.30	97.44
ash	7.71	8.03
Amino acids (g/kg dry matter)		
lysine	30.5	7.71
methionine	6.94	6.01
threonine	15.85	13.21
tryptophan	4.01	3.98
cysteine	4.23	4.66
leucine	28.0	24.55
isoleucine	18.9	14.77
histidine	9.78	8.98
arginine	17.51	20.98
phenylalanine	18.53	19.31
Minerals (g/kg)		
calcium	4.11	2.98
phosphorous	4.87	9.44
magnesium	1.77	1.69
iron	0.111	0.099
zinc	0.071	0.066
copper	0.01	0.012

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Galactomyces Ferment Filtrate		Hydrolyzed Candida Saitoana Extract		Hydrolyzed Yeast		Hydrolyzed Yeast Extract	
Totals*	**77**	**0.072 – 90.7**	**10**	**0.02 – 3.8**	**2**	**0.00038 – 0.004**	**26**	**0.000018 – 0.035**
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*70*	*0.072 – 90.7*	*9*	*0.02 – 3.8*	*2*	*0.00038 – 0.004*	*25*	*0.00003 – 0.035*
Rinse-Off	*7*	*5*	*1*	*NR*	*NR*	*NR*	*1*	*0.000018 – 0.0011*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type*								
Eye Area	5	0.072 – 37.5	2	0.02	NR	0.0005	1	NR
Incidental Ingestion	NR	NR	NR	NR	1	NR	NR	NR
Incidental Inhalation-Spray	31[a]; 24[b]	NR	2[a]; 4[b]	NR	1[a]	NR	10[a]; 13[b]	0.00043 – 0.0035[a]
Incidental Inhalation-Powder	24[b]	1.1	4[b]	3.8[c]	NR	0.0005[c]	13[b]	0.02[c]
Dermal Contact	76	1.1 – 90.7	10	0.02 – 3.8	1	0.00038 – 0.004	26	0.00003 – 0.02
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	1	NR	NR	NR	NR	NR	NR	0.000035 – 0.035
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	0.000018 – 0.000035
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	3	NR	NR	NR	1	NR	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
as reported by product category								
Baby Products								
Baby Lotions/Oils/Powders/Creams								
Eye Makeup Preparations								
Eyeliner								
Eye Shadow								
Eye Lotion	4	37.5	1	0.02	NR	0.0005		
Eye Makeup Remover								
Mascara	NR	0.072						
Other Eye Makeup Preparations	1	NR	1	NR			1	NR
Fragrance Preparations								
Cologne and Toilet Water								
Hair Preparations (non-coloring)								
Hair Conditioner							NR	0.0011
Hair Spray (aerosol fixatives)								
Permanent Waves								
Shampoos (non-coloring)	1	NR					NR	0.000035
Tonics, Dressings, and Other Hair Grooming Aids							NR	0.00043 – 0.0035
Wave Sets								
Other Hair Preparations							NR	0.035
Hair Coloring Preparations								
Hair Dyes/Colors (all types requiring caution statements and patch tests)							NR	0.000018
Hair Rinses (coloring)							NR	0.000035
Makeup Preparations								
Blushers (all types)								
Face Powders	NR	1.1						
Foundations	NR	17.6			NR	0.00038		
Lipstick					1	NR		
Makeup Bases								

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Rouges								
Makeup Fixatives								
Other Makeup Preparations	1	NR						
Manicuring Preparations (Nail)								
Other Manicuring Preparations								
Oral Hygiene Products								
Dentifrices								
Personal Cleanliness Products								
Bath Soaps and Detergents	1	NR						
Deodorants (underarm)								
Feminine Deodorants	1	NR						
Other Personal Cleanliness Products	1	NR						
Shaving Preparations								
Aftershave Lotion								
Other Shaving Preparations								
Skin Care Preparations								
Cleansing	4	5	1	NR			1	NR
Depilatories								
Face and Neck (exc shave)	23	NR	4	3.8 (not spray)	NR	0.0005 (not spray)	10	0.02 (not spray)
Body and Hand (exc shave)							3	NR
Moisturizing	24	90.7 (not spray)	1	0.02 (not spray)	1	NR	7	NR
Night		83.1 (not spray)	1	NR			1	NR
Paste Masks (mud packs)								
Skin Fresheners	7	NR					2	NR
Other Skin Care Preparations	9	NR	1	0.02	NR	0.004	1	0.00003
Suntan Preparations								
Suntan Gels, Creams, and Liquids								
	Kluyveromyces Extract		**Pichia Anomala Extract**		**Pichia Ferment Lysate Filtrate**		**Saccharomyces Cerevisiae Extract**	
Totals*	**5**	**NR**	**2**	**0.05 – 0.1**	**3**	**NR**	**56**	**0.0001 – 0.3**
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*5*	*NR*	*2*	*0.05 – 0.1*	*3*	*NR*	*50*	*0.001 – 0.18*
Rinse-Off	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*6*	*0.0001 – 0.3*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NR	NR	NR	NR	NR	16	0.00083 – 0.15
Incidental Ingestion	NR	NR	NR	NR	NR	NR	1	NR
Incidental Inhalation-Spray	1[a]; 1[b]	NR	2[a]	NR	1[a]; 2[b]	NR	11[a]; 18[b]	0.045; 0.1[a]
Incidental Inhalation-Powder	1[a]	NR	NR	NR	2[b]	NR	2; 18[b]	0.001 – 0.18[c]
Dermal Contact	5	NR	2	0.05 – 0.1	3	NR	50	0.00083 – 0.3
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	NR	NR	NR	4	0.0001 – 0.001
Hair-Coloring	NR	NR	NR	NR	NR	NR	1	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	NR	NR	NR	NR	NR	NR	1	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
as reported by product category								
Baby Products								
Baby Lotions/Oils/Powders/Creams								
Eye Makeup Preparations								
Eyeliner								
Eye Shadow								
Eye Lotion	9	0.0005 – 0.0036					6	0.001 – 0.15
Eye Makeup Remover							NR	0.00083
Mascara								
Other Eye Makeup Preparations	6	NR	1	NR			10	NR
Fragrance Preparations								
Cologne and Toilet Water								
Hair Preparations (non-coloring)								
Hair Conditioner	4	0.005					NR	0.001
Hair Spray (aerosol fixatives)								
Permanent Waves								
Shampoos (non-coloring)	2	0.00025					4	0.0001
Tonics, Dressings, and Other Hair Grooming Aids	2	NR						
Wave Sets								
Other Hair Preparations	1	0.005						
Hair Coloring Preparations								
Hair Dyes/Colors (all types requiring caution statements and patch tests)							1	NR
Hair Rinses (coloring)								
Makeup Preparations								
Blushers (all types)								
Face Powders							2	NR
Foundations	NR	0.000038						
Lipstick							1	NR
Makeup Bases								
Rouges								
Makeup Fixatives								
Other Makeup Preparations							1	NR
Manicuring Preparations (Nail)								
Other Manicuring Preparations								
Oral Hygiene Products								
Dentifrices								
Personal Cleanliness Products								
Bath Soaps and Detergents								
Deodorants (underarm)								
Feminine Deodorants								
Other Personal Cleanliness Products								
Shaving Preparations								
Aftershave Lotion	1	NR					NR	0.025
Other Shaving Preparations	1	NR						
Skin Care Preparations								
Cleansing	4	NR					1	0.3
Depilatories								
Face and Neck (exc shave)	40	0.0005 – 0.12 (not spray)	1	NR	2	NR	18	0.001 – 0.18 (not spray)

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Body and Hand (exc shave)	3	0.19 (not spray)					NR	0.01 (not spray)
Moisturizing	19	NR	2	0.1 (not spray)	1	NR	9	0.045 (spray)
Night	4	0.002 (not spray)	NR	0.05 (not spray)			2	0.045 (not spray)
Paste Masks (mud packs)								
Skin Fresheners	2	NR					NR	0.1
Other Skin Care Preparations	11	NR					1	0.09
Suntan Preparations								
Suntan Gels, Creams, and Liquids								
	Saccharomyces Ferment		**Saccharomyces Ferment Extract Lysate Filtrate**		**Saccharomyces Ferment Filtrate**		**Saccharomyces Ferment Lysate Filtrate**	
Totals*	**42**	**0.00013 – 1.2**	**NR**	**0.25**	**48**	**0.01 – 8**	**38**	**0.0035**
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*38*	*0.00013 – 1.2*	*NR*	*0.25*	*39*	*0.03 – 0.065*	*37*	*0.0035*
Rinse-Off	*4*	*0.002*	*NR*	*NR*	*9*	*0.01 – 8*	*1*	*0.0035*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	3	NR	NR	NR	NR	NR	6	NR
Incidental Ingestion	NR	0.00013	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	20[a]; 1[b]	NR	NR	NR	16[a]; 12[b]	0.065; 0.03[a]; 0.038[b]	2; 12[a]; 14[b]	NR
Incidental Inhalation-Powder	1[b]	NR	NR	NR	1; 12[b]	0.038[b]	14[b]	NR
Dermal Contact	41	0.72 – 1.2	NR	0.25	48	0.01 – 2.1	36	0.0035
Deodorant (underarm)	8[a]	NR	NR	NR	4[a]	NR	NR	NR
Hair - Non-Coloring	1	0.002	NR	NR	NR	0.03 – 8	2	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	1	0.00013	NR	NR	2	0.01 – 0.038	NR	NR
Baby Products	NR	NR	NR	NR	NR	NR	NR	NR
as reported by product category								
Baby Products								
Baby Lotions/Oils/Powders/Creams								
Eye Makeup Preparations								
Eyeliner								
Eye Shadow							1	NR
Eye Lotion	2	NR					3	NR
Eye Makeup Remover								
Mascara								
Other Eye Makeup Preparations	1	NR					2	NR
Fragrance Preparations								
Cologne and Toilet Water					NR	0.065		
Hair Preparations (non-coloring)								
Hair Conditioner	NR	0.002			NR	8		
Hair Spray (aerosol fixatives)							2	NR
Permanent Waves								
Shampoos (non-coloring)	1	NR						
Tonics, Dressings, and Other Hair Grooming Aids					NR	0.03		
Wave Sets								
Other Hair Preparations								

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Hair Coloring Preparations								
Hair Dyes/Colors (all types requiring caution statements and patch tests)								
Hair Rinses (coloring)								
Makeup Preparations								
Blushers (all types)	NR	1.2						
Face Powders					1	NR		
Foundations					NR	0.045		
Lipstick	NR	0.00013						
Makeup Bases								
Rouges							1	NR
Makeup Fixatives								
Other Makeup Preparations							1	NR
Manicuring Preparations (Nail)								
Other Manicuring Preparations								
Oral Hygiene Products								
Dentifrices								
Personal Cleanliness Products								
Bath Soaps and Detergents	8	NR						
Deodorants (underarm)					4	NR		
Feminine Deodorants					NR	0.038		
Other Personal Cleanliness Products	1	NR			2	0.01		
Shaving Preparations								
Aftershave Lotion								
Other Shaving Preparations								
Skin Care Preparations								
Cleansing	2	NR			5	2.1	1	0.0035
Depilatories								
Face and Neck (exc shave)					11	NR	13	NR
Body and Hand (exc shave)	1	NR			1	NR	1	NR
Moisturizing	19	NR	NR	0.25 (not spray)			12	NR
Night					15	NR		
Paste Masks (mud packs)								
Skin Fresheners					2	NR		
Other Skin Care Preparations	6	0.72			6	NR	1	NR
Suntan Preparations								
Suntan Gels, Creams, and Liquids	1	NR			1	NR		

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
	Saccharomyces Lysate		Saccharomyces Lysate Extract		Schizosaccharomyces Ferment Filtrate		Yeast	
Totals*	**14**	**NR**	**81**	**0.0007 – 0.71**	**5**	**NR**	**11**	**NR**
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*8*	*NR*	*76*	*0.01 – 0.71*	*5*	*NR*	*10*	*NR*
Rinse-Off	*6*	*NR*	*5*	*0.0007 – 0.0025*	*NR*	*NR*	*1*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type								
Eye Area	1	NR	10	0.013 – 0.67	NR	NR	NR	NR
Incidental Ingestion	6	NR	NR	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	3[a]; 3[b]	NR	20[a]; 26[b]	NR	2[a]; 1[b]	NR	1[b]	NR
Incidental Inhalation-Powder	3[b]	NR	26[b]	0.01 – 0.71[c]	1[b]	NR	1[b]	NR
Dermal Contact	8	NR	78	0.0023 – 0.71	5	NR	11	NR
Deodorant (underarm)	NR	NR	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	3	0.0007 – 0.002	NR	NR	NR	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR	NR	NR
Mucous Membrane	6	NR	NR	NR	NR	NR	NR	NR
Baby Products	NR	NR	NR	0.067	NR	NR	NR	NR
as reported by product category								
Baby Products								
Baby Lotions/Oils/Powders/Creams			NR	0.067				
Eye Makeup Preparations								
Eyeliner								
Eye Shadow								
Eye Lotion			1	0.013 – 0.67				
Eye Makeup Remover								
Mascara								
Other Eye Makeup Preparations	1	NR	9	NR				
Fragrance Preparations								
Cologne and Toilet Water								
Hair Preparations (non-coloring)								
Hair Conditioner			1	0.0007 – 0.002				
Hair Spray (aerosol fixatives)								
Permanent Waves								
Shampoos (non-coloring)			1	0.0007 – 0.002				
Tonics, Dressings, and Other Hair Grooming Aids			1	NR				
Wave Sets								
Other Hair Preparations								
Hair Coloring Preparations								
Hair Dyes/Colors (all types requiring caution statements and patch tests)								
Hair Rinses (coloring)								
Makeup Preparations								
Blushers (all types)								
Face Powders								
Foundations			1	NR				
Lipstick								
Makeup Bases			1	NR				

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Rouges								
Makeup Fixatives			1	NR				
Other Makeup Preparations			1	0.23				
Manicuring Preparations (Nail)								
Other Manicuring Preparations								
Oral Hygiene Products								
Dentifrices	6	NR						
Personal Cleanliness Products								
Bath Soaps and Detergents								
Deodorants (underarm)								
Feminine Deodorants								
Other Personal Cleanliness Products								
Shaving Preparations								
Aftershave Lotion			1	NR				
Other Shaving Preparations			2	NR				
Skin Care Preparations								
Cleansing			NR	0.0023 – 0.0025				
Depilatories								
Face and Neck (exc shave)	3	NR	25	0.18 – 0.71 (not spray)	1	NR	1	NR
Body and Hand (exc shave)			1	0.01 (not spray)				
Moisturizing	3	NR	15	0.025 (not spray)	2	NR		
Night			3	NR				
Paste Masks (mud packs)			1	NR			1	NR
Skin Fresheners			1	NR				
Other Skin Care Preparations	1	NR	15	NR	2	NR	9	NR
Suntan Preparations								
Suntan Gels, Creams, and Liquids								
	Yeast Extract		**Yeast Ferment Extract**					
Totals*	**398**	**0.0000036 – 0.16**	**15**	**NR**				
summarized by likely duration and exposure**								
Duration of Use								
Leave-On	*343*	*0.0000036 – 0.16*	*12*	*NR*				
Rinse-Off	*55*	*0.0001 – 0.01*	*3*	*NR*				
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*				
Exposure Type								
Eye Area	25	0.001 – 0.15	NR	NR				
Incidental Ingestion	1	0.00072 – 0.002	NR	NR				
Incidental Inhalation-Spray	2; 125[a]; 133[b]	0.065; 0.00001 – 0.03[a]; 0.038[b]	6[a]; 4[b]	NR				
Incidental Inhalation-Powder	133[b]	0.0000036 – 0.021; 0.038[b]; 0.0036 – 0.16[c]	4[b]	NR				
Dermal Contact	334	0.0000036 – 0.16	14	NR				
Deodorant (underarm)	NR	NR	NR	NR				
Hair - Non-Coloring	62	0.0001 – 0.03	1	NR				
Hair-Coloring	NR	NR	NR	NR				
Nail	1	NR	NR	NR				
Mucous Membrane	1	0.0007 – 0.038	1	NR				
Baby Products	NR	NR	NR	NR				

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Baby Products								
Baby Lotions/Oils/Powders/Creams								
Eye Makeup Preparations								
Eyeliner	NR	0.002						
Eye Shadow	NR	0.001 – 0.002						
Eye Lotion	12	0.038 – 0.15						
Eye Makeup Remover	NR	0.0048 – 0.0048						
Mascara	NR	0.024						
Other Eye Makeup Preparations	13	NR						
Fragrance Preparations								
Cologne and Toilet Water	NR	0.065						
Hair Preparations (non-coloring)								
Hair Conditioner	22	0.0001						
Hair Spray (aerosol fixatives)	2	NR						
Permanent Waves	NR	0.01						
Rinses (non-coloring)								
Tonics, Dressings, and Other Hair Grooming Aids	13	0.009 – 0.03						
Wave Sets								
Other Hair Preparations	11	0.01	1	NR				
Hair Coloring Preparations								
Hair Dyes/Colors (all types requiring caution statements and patch tests)								
Hair Rinses (coloring)								
Makeup Preparations								
Blushers (all types)								
Face Powders	NR	0.0000036 – 0.021						
Foundations	5	0.0014 – 0.038						
Lipstick	NR	0.00072 – 0.002						
Makeup Bases	6	NR						
Rouges								
Makeup Fixatives	1	NR						
Other Makeup Preparations	4	NR						
Manicuring Preparations (Nail)								
Other Manicuring Preparations								
Oral Hygiene Products								
Dentifrices								
Personal Cleanliness Products								
Bath Soaps and Detergents	NR	0.0007	1	NR				
Deodorants (underarm)								
Feminine Deodorants	NR	0.038						
Other Personal Cleanliness Products	NR	0.01						
Shaving Preparations								
Aftershave Lotion	NR	0.025						
Other Shaving Preparations	1	NR						
Skin Care Preparations								
Cleansing	12	0.0007 – 0.0036	2	NR				
Depilatories								
Face and Neck (exc shave)	117	0.0036 – 0.16 (not spray)	4	NR				

Table 6. Frequency (2023)[35] and concentration (2021/2023)[36,122,123] of use according to likely duration and exposure and by product category

	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)	# of Uses	Max Conc of Use (%)
Body and Hand (exc shave)	16	0.0074 – 0.042 (not spray)						
Moisturizing	83	NR	6	NR				
Night	22	NR						
Paste Masks (mud packs)	5	NR						
Skin Fresheners	6	0.00001 – 0.0036						
Other Skin Care Preparations	31	0.0036 – 0.14	1	NR				
Suntan Preparations								
Suntan Gels, Creams, and Liquids								

NR – not reported

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

**likely duration and exposure is derived based on product category (see Use Categorization https://www.cir-safety.org/cir-findings)

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

[b] Not specified whether a spray or a powder, but it is possible the use can be as a spray or a powder, therefore the information is captured in both categories

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

Table 7. Yeast-derived not reported to be use according to 2023 frequency of use and 2021/2023 concentration of use data

Hydrolyzed Candida Bombicola Extract	Pichia Heedii Extract
Hydrolyzed Kluyveromyces Extract	Pichia Minuta Extract
Hydrolyzed Metschnikowia Agaves Extract	Pichia Pastoris Ferment Filtrate
Hydrolyzed Metschnikowia Reukaufii Extract	Phaffia Rhodozyma Extract
Hydrolyzed Metschnikowia Shanxiensis Extract	Phaffia Rhodozyma Ferment Extract
Hydrolyzed Saccharomyces Cell Wall	Saccharomyces
Hydrolyzed Saccharomyces Extract	Saccharomyces Extract
Hydrolyzed Saccharomyces Lysate Extract	Saccharomyces Ferment Extract
Hydrolyzed Torulaspora Delbruekii Extract	Saccharomyces Ferment Lysate Extract
Lactic Yeasts	Saccharomyces Lysate Extract Filtrate
Lipomyces Lipid Bodies	Saccharomyces Lysate Filtrate
Lipomyces Oil	Schizosaccharomyces Ferment Extract Filtrate
Lipomyces Oil Extract	Schizosaccharomyces Pombe Extract
Metschnikowia Agaves Extract	Torulaspora Delbrueckii Extract
Metschnikowia Henanensis Extract	Torulaspora Delbrueckii Ferment
Metschnikowia Reukaufii Lysate Extract	Yarrowia Lipolytica Extract
Metschnikowia Viticola Extract	Yarrowia Lipolytica Ferment Lysate
Pichia Caribbica Ferment	Yarrowia Lipolytica Oil
Pichia Extract	
Pichia Ferment Extract Filtrate	

Table 8. Food use/presence and non-cosmetic uses of yeast species

Associated Ingredients	Food Use/Presence	Other Non-Cosmetic Uses	Reference
Galactomyces Ferment Filtrate	*Geotrichum candidum* is used as an adjunct culture in the maturation of cheese *Galactomyces geotrichum* is found in alcohols and dairy products	*Galactomyces geotrichum* is used in biodegradation and bioremediation processes	124,125
Hydrolyzed Candida Bombicola Extract	*Starmerella bombicola* is naturally present in concentrated grape juice and in high-sugar fermented vegetables and honey	*Candida bombicola* produces sophorolipids which may be used as a biosurfactant in food, pharmaceutical, and cleaning industries	126
Hydrolyzed Candida Saitoana Extract	*Candida saitoana* may be found in plant-based fermented foods	*Candida saitoana* is used as a biocontrol treatment of post-harvest disease in apples and citrus fruit	127,128
Hydrolyzed Kluyveromyces Extract Kluyveromyces Extract	*Kluyveromyces marxianus* is present in Korean kefir and other dairy products Lactase enzyme preparation from *Kluyveromyces lactis* is GRAS for use in hydrolyzing lactose in milk [21CFR184] Rennet and chymosin preparation from *Kluyveromyces marxianus* to coagulate milk in cheeses and other dairy products is considered GRAS [21CFR184] *Kluyveromyces lactis* - QPS status *Kluyveromyces marxianus* – QPS status	*Kluyveromyces marxianus* is used in biotechnological (e.g., native enzyme production, inulinase production) and environmental applications (e.g., heavy metal recovery from agricultural industry wastewater) *Kluyveromyces marxianus* may be used as a probiotic	44,129-132
Hydrolyzed Metschnikowia Agaves Extract Metschnikowia Agaves Extract	*Metschnikowia agaves* can be found in blue agave used to make tequila	-	133
Hydrolyzed Metschnikowia Reukaufii Extract Metschnikowia Reukaufii Lysate Extract Yeast Extract derived from *Metschnikowia reukaufii*	*Metschnikowia reukaufii* is used in beer fermentation	-	134
Hydrolyzed Saccharomyces Cell Wall Saccharomyces Cerevisiae Extract	*Saccharomyces bayanus* is used in wine and beer-making *Saccharomyces cerevisiae* is used in baking and alcohol production as a fermentative agent Baker's yeast extract (mechanically ruptured cells of *Saccharomyces cerevisiae*) is GRAS as a flavoring agent and adjuvant at a level not to exceed 5% in food [21CFR184.1983] Dried yeast (*Saccharomyces cerevisiae*) is considered to be GRAS as a multipurpose food additive [21CFR172.896] Baker's yeast glycan (derived from dried cell walls of *Saccharomyces cerevisiae*) is approved as a direct food additive for human consumption when used as described in 21CFR172.898 (e.g., not to exceed a concentration of 5% in finished salad dressing) *Saccharomyces cerevisiae* – QPS status *Saccharomyces pastorianus* is used in the production of lager beer	Inactivated yeast (*Saccharomyces cerevisiae*) cells are used in animal feed and over-the-counter nutritional supplements	38,132,135
Hydrolyzed Torulaspora Delbrueckii Extract Torulaspora Delbrueckii Extract Torulaspora Delbrueckii Ferment	*Torulaspora delbrueckii* is used in the production of breads/bakery products, chocolate, coffee, and fermented beverages *Torulaspora delbrueckii* may be present in cheese	-	136-138
Lipomyces Oil Lipomyces Oil Extract	*Lipomyces starkeyi* is GRAS in probiotics	-	132,139
Metschnikowia Viticola Extract	*Metschnikowia viticola may be present in wine*	-	140,141

Table 8. Food use/presence and non-cosmetic uses of yeast species

Associated Ingredients	Food Use/Presence	Other Non-Cosmetic Uses	Reference
	Metschnikowia viticola has been isolated from grapes grown in Hungary		
Pichia Anomala Extract	*Wickerhamomyces anomalus* is used in Chinese liquor production and soy sauce *Pichia anomala* is commonly found in fermented food and beverages and may be used as a food-flavoring agent *Pichia anomala* – QPS status	*Pichia anomala* may be used as a biopreservative	132,142-145
Pichia Caribbica Ferment	Kombucha tea culture is a symbiosis of several substances, including *Pichia caribbica* *Pichia caribbica* may be used in the production of alcoholic beverages *Pichia caribbica* has been isolated from Brazilian fermented table olives	*Picha caribbica* may be used to produce malic acid	146-148
Pichia Ferment Extract Filtrate Pichia Pastoris Ferment Filtrate	The following substances are considered GRAS: -Pepsin A enzyme preparation produced by *Pichia pastoris* to overexpress the gene encoding pepsin A -Myoglobin preparation from a strain of *Pichia pastoris* expressing the myoglobin gene from *Bos taurus* (cattle) -Soy leghemoglobin preparation from a strain of *Pichia pastoris* -Soybean leghemoglobin from *Pichia pastoris* -Phospholipase C enzyme preparation from *Pichia pastoris* expressing a heterologous phospholipase C gene *Pichia pastoris* – QPS status	-	149
Pichia Ferment Lysate Filtrate	-	-*Pichia stipitis* is capable of fermenting glucose, xylose, galactose, cellulobiose, and fermentose -*Pichia stipitis* may be used in the production of bioethanol -*Pichia populi* has been used in the production of arabitol-free xylitol	150-154
Pichia Heedii Extract	-	*Pichia heedii* may be used to assimilate D-xylose	155
Pichia Minuta Extract	*Pichia minuta* may be found in wine	*Pichia minuta* has been isolated from olive tree cultures	156,157
Phaffia Rhodozyma Extract Phaffia Rhodozyma Ferment Extract	*Phaffia rhodozyma* – QPS status	Astaxanthin-rich *Phaffia rhodozyma* may be used in feed for salmon and trout	132,158
Schizosaccharomyces Pombe Extract	*Schizosaccharomyces pombe* is used in cachaça (alcoholic beverage made from fermented sugarcane juice) and kombucha *Schizosaccharomyces pombe* – QPS status	-	132,136
Yarrowia Lipolytica Extract Yarrowia Lipolytica Ferment Lysate Yarrowia Lipolytica Oil	*Yarrowia lipolytica* has been found in a variety of different cheeses; predominantly ewe, goat, and buffalo cheese *Yarrowia lipolytica* is also found in other fermented dairy (e.g., yogurt) and meat (e.g., salami) products Eicosapentaenoic acid -rich triglyceride oil *from Yarrowia lipolytica* is considered GRAS at a maximum intake of 3.0 g per person per day eicosapentaenoic acid and not to be combined or augmented with any other food ingredient containing eicosapentaenoic acid and/or another omega-3 fatty acid, docosahexaenoic acid [21 CFR 184.1472] *Yarrowia lipolytica* – QPS status	*Yarrowia lipolytica* is used in livestock feed, a biotechnological production host for organic acids or hydrophobic substances or carotenoids, a heterologous production host for pharmaceutical and industrial proteins and enzymes, for the mass production of biofuels, and for bioremediation purposes Oil produced by *Yarrowia lipolytica* may be used in the agro-alimentary, pharmaceutical, and bioenergy industry *Yarrowia lipolytica* may be used for commercial production of food grade citric acid [21 CFR 173.165]	132,159,160

Table 8. Food use/presence and non-cosmetic uses of yeast species

Associated Ingredients	Food Use/Presence	Other Non-Cosmetic Uses	Reference
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* is naturally found on plant tissues that are commonly consumed (e.g., apples) – this species is also used in fruits to control fungal pathogens *Candida oleophila* may be present in alcoholic beverages	-	42,128
Yeast Extract (when derived from *Candida magnoliae*)	*Candida magnoliae* has been isolated from lime honey and honeycomb	-	161-163
Yeast Extract (when derived from *Debaryomyces nepalensis*)	*Debaryomyces nepalensis* has been isolated from persimmon fruit, passion fruit, avocado, and cape gooseberry	*Debaryomyces nepalensis* may be used in the production of solutes, haloenzymes, alcoholic beverages, and in biological waste treatment *Debaryomyces nepalensis* may be used as a biocontrol agent in fruit and cheese *Debaryomyces nepalensis* may be used in the production of xylitol	164-169
Yeast Extract (when derived from *Metschnikowia pulcherrima*)	*Metschnikowia pulcherrima* may be present in alcoholic beverages and coffee	*Metschnikowia pulcherrima* may be used to produce D-arabitol	170,171

GRAS = generally recognized as safe; QPS = qualified presumption of safety

Table 9. In vitro dermal absorption studies

Ingredient	Test Article	Concentration/Dose	Protocol	Results	References
Metschnikowia Agaves Extract	emulsion containing Metschnikowia Agaves Extract	30%	OECD TG 428	Absorption of 2.4% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Pichia Anomala Extract	emulsion containing Pichia Anomala Extract	30%	OECD TG 428	Absorption of 0.7% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Pichia Anomala Extract	emulsion containing Pichia Anomala Extract	30%	OECD TG 428	Absorption of 0.41% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Pichia Heedii Extract	emulsion containing Pichia Heedii Extract	30%	OECD TG 428	Absorption of 0.2% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Pichia Minuta Extract	emulsion containing Pichia Minuta Extract	30%	OECD TG 428	Absorption of 0.6% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Yeast Extract (may also be chemically similar to Hydrolyzed Candida Saitoana Extract)	emulsion containing Yeast Extract derived from *Candida saitoana*	30%	OECD TG 428	Absorption of 1.1% of the total quantity applied to the surface of the epidermis after 24 h	[20]
Yeast Extract (may also be chemically similar to Hydrolyzed Metschnikowia Reukaufii Extract)	emulsion containing Yeast Extract derived from *Metschnikowia reukaufii*	30%	OECD TG 428	Absorption of 4.6% of the total quantity applied to the surface of the epidermis after 24 h	[20]

NR = not reported; OECD TG = Organisation for Economic Co-operation and Development test guidelines

Table 10. Acute toxicity studies*

Ingredient	Test Article	Vehicle	Test Population	Concentration/Dose	Protocol	LD_{50}/LC_{50}/Results	Reference
IN VITRO							
Pichia Minuta Extract	Pichia Minuta Extract	NR	murine fibroblast cell line, BALB/c 3T3 cells, clone 31	8 test concentrations (specific concentrations not stated)	3T3 neutral red uptake assay; OECD TG 129	LD_{50} > 2000 mg/kg	[39]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract (derived from *Pichia naganishii*)	NR	murine fibroblast cell line, BALB/c 3T3 cells, clone 31	8 test concentrations (specific concentrations not stated)	3T3 neutral red uptake assay; OECD TG 129	LD_{50} > 2000 mg/kg	[39]
ANIMAL							
Dermal							
Hydrolyzed Saccharomyces Cell Wall	90% *Saccharomyces cerevisiae* cell wall (containing 24% glucan and 7% mannan)**	10% HSCAS	Sprague-Dawley rats (5/sex/group)	2000 mg/kg bw; 55% dilution (final test concentration of 49.5% yeast cell wall)	Test article applied to gauze pad and placed on clipped, dorsal/trunk area of animal; pads wrapped; 24 h administration period; 14 d evaluation period	No mortalities or signs or gross toxicity, dermal irritation, adverse pharmacological effects, or abnormal behaviors were noted. The acute dermal LD_{50} of a 55% dilution of the test article was determined to be > 2000 mg/kg bw.	[4]
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract**	Water	Crl:WI (Han) rats (5/sex)	2000 mg/kg	OECD TG 402; occlusive conditions; 24 h administration period; observation for 14 d	Two males and two females showed chromodacryorrhoea on day 1 (24 h after treatment). In addition, one male showed hunched posture on day 1. Two females had scales or focal erythema in the treated skin area during the observation period. No other abnormalities were noted; LD_{50} was determined to be > 2000 mg/kg bw.	[2]

Table 10. Acute toxicity studies*

Ingredient	Test Article	Vehicle	Test Population	Concentration/Dose	Protocol	LD_{50}/LC_{50}/Results	Reference
				Oral			
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate**	NR	ddY-N mice (10/sex/group)	34,730, 41,670, 50,000, 60,000 mg/kg	Administration via gavage	No mortality or adverse effects observed; LD_{50} determined to be > 60,000 mg/kg	40
Hydrolyzed Yeast	Yeast hydrolysate obtained from *Saccharomyces cerevisiae***	NR	Sprague-Dawley rats (5/sex/group)	5000 mg/kg bw	OECD TG 420; gavage administration; 14-d observation period	No mortality or adverse effects observed.	31
Hydrolyzed Saccharomyces Cell Wall	90% *Saccharomyces cerevisiae* cell wall (containing 24% glucan and 7% mannan)**	10% HSCAS and distilled water	Sprague-Dawley rats (5/sex/group)	2000 mg/kg bw; 55% dilution (final test concentration of 49.5% yeast cell wall)	Administration via gavage; 14-d observation period	No mortalities were observed throughout the study. One female exhibited reduced fecal volume, however, this animal recovered by day 2. No other signs of toxicity were noted.	4
Saccharomyces Ferment	Fermentate powder derived from *Saccharomyces cerevisiae***	methylcellulose and water	Sprague-Dawley rats (10/sex/group)	2000 mg/kg bw	OECD TG 423; gavage administration; 14-d observation period	No signs of toxicity observed.	41
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* strain O**	NR	rats (species, sex, and number of animals not specified)	2.3 - 3.8 x 10^8 CFU	Animals given single oral dose of the test substance (method of oral administration not stated). Animals were observed for 22 d.	Test substance was not considered to be toxic, infective, or pathogenic	42
				Inhalation			
Hydrolyzed Saccharomyces Cell Wall	90% *Saccharomyces cerevisiae* cell wall (containing 24% glucan and 7% mannan)**	10% HSCAS and distilled water	Sprague-Dawley rats (5/sex/group)	Gravimetric and nominal chamber concentrations were 2.09 and 5.81 mg/l, respectively	OECD TG 403; mass median aerodynamic diameter estimated to be 3.75 µm; 14-d observation period	Two males and 2 females exhibited irregular respiration and hypoactive behavior following exposure; however, these animals recovered by day 5. No gross abnormalities were observed upon necropsy, and no other adverse effects were noted; LC_{50} was determined to be > 2.09 mg/l in male and female rats.	4
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* strain O**	NR	rats (species, sex, and number of animals not specified)	1.2 -5.2 x 10^8 CFU	Animals exposed to test substance via intratracheal route and observed for 22 d	Test substance was not considered to be toxic, infective, or pathogenic	42
				Parenteral			
Pichia Ferment Extract Filtrate and Pichia Pastoris Ferment Filtrate	Live *Pichia pastoris* cells**	sterile saline	female BALB/c mice (20/group)	1 × 10^6 CFU	Intravenous administration of the test substance via the lateral tail vein; control group one received inoculation with saline; control group two was left untreated; body weight and behavior monitored; 5 mice/group were euthanized at 4, 24, and 48 h and 6 d post-administration; samples of sera and tissues (kidney, liver, brain, spleen, heart, and lung) were collected	Results were similar among control and treated groups (no adverse effects relating to body weight, survival, or locomotion changes); no adverse effects related to pathology in tissues were noted	43
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* strain O**	NR	rats (species, sex, and number of animals not specified)	1.1-2.0 x 10^7 CFU	Animals subcutaneously injected with test substance and observed for 22 d	Test substance was not considered to be toxic, infective, or pathogenic	42

CFU = colony-forming units; LC_{50} = median lethal concentration; LD_{50} = median lethal dose; NR = not reported; OECD TG = Organisation for Economic Co-operation and Development test guidelines

*It should be noted that the test articles evaluated in these studies may not be identical to the wINCI ingredients reviewed in this report; however, as they may be similar, both test articles and potentially-related wINCI ingredients have been included in the table

**unknown if test substance is a cosmetic ingredient (e.g., *Candida oleophila* strain O); however, ingredient relates to INCI ingredient reviewed in this report (Yeast Extract (when derived from *Candida oleophila*)

Table 11. Repeated dose oral toxicity studies*

Ingredient	Test Article	Vehicle	Animals/Group	Study Duration	Dose/Concentration	Protocol	Results	Reference
Hydrolyzed Yeast	Yeast hydrolysate obtained from *Saccharomyces cerevisiae***	NR	Sprague-Dawley rats (5/sex/group)	14 d	1000 mg/kg bw/d	OECD TG 407; animals administered test substance orally (method of oral administration not stated); animals killed after treatment period; control animals given water; satellite group treated with the test substance, at the same dose, at the same time period, and kept for another 14 d post-treatment for observation	No significant differences in organ weights between control and treated groups were noted. No adverse hematological effects, gross abnormalities, or histopathological changes were observed. Treatment with the test substance induced significant increases in body weight compared to the control group ($p < 0.05$).	31
Kluyveromyces Extract	*Kluyveromyces marxianus* strains A4 and A5**	sterilized saline	female SPF BALB/c mice (6/group)	14 d	1.0 x 10^6 CFU/ml or 1.0 x 10^8 CFU/ml	Animals were orally administered the test substance (method of oral administration not stated); negative control group left untreated; another negative control group treated with saline only	No adverse effects relating to body weight or food and water intake were observed. The spleen to body ratio of the A5 strain (high concentration)-treated group was significantly lower than that of the untreated negative control group ($p < 0.05$). The liver to body weight ration of the A4 strain (low concentration)-treated group was significantly lower than that of the untreated negative control group ($p < 0.05$). All blood parameters and cytokine parameters (interleukin-1β and tumor necrosis factor-α) were comparable between treated and negative control groups.	44
Phaffia Rhodozyma Extract and Phaffia Rhodozyma Ferment Extract	*Phaffia rhodozyma* extract**	corn oil	Sprague-Dawley rats (6/sex/group)	28 d	3 ml/kg; 500 and 1000 mg/kg	OECD TG 407; gavage administration 6 d/wk; control group given corn oil	Decreased body weight was observed in females in the 1000 mg/kg treated group; increased ALT levels and relative liver weights were observed in females in the 1000 mg/kg group ($p < 0.05$); absolute and relative thymus weights tended to increase in males of the 1000 mg/kg group; no other toxicologically-relevant adverse effects were observed; NOAEL > 1000 mg/kg	45
Saccharomyces Ferment	Fermentate powder derived from *Saccharomyces cerevisiae***	methylcellulose and water	Sprague-Dawley rats (20/sex/group)	90 d	30, 200, and 1500 mg/kg bw/d	OECD TG 408; gavage treatment once per day; control group used, however, details regarding treatment not provided	No treatment-related toxicity was observed regarding general state, behavior, external appearance, body weight, ophthalmologic changes, urine analysis, organ weights, or histopathology. A dose-related slight decrease in total cholesterol was observed in male rats of the high-dose (not observed in females); NOAEL = 1500 mg/kg bw/d	41
Saccharomyces Ferment	Fermentate powder derived from *Saccharomyces cerevisiae***	methylcellulose and water	Sprague-Dawley rats (20/sex/group)	1 yr	20, 200, and 800 mg/kg bw/d	OECD TG 408 and 452; gavage administration; control group used, however, details regarding treatment not provided	No macroscopic or microscopic, serum chemistry, hematological, urinary, or histological adverse effects were observed to be of clinical significance. A statistically significant decrease in water consumption over nonconsecutive weeks was observed in the highest dose group; NOAEL = 800 mg/kg bw/d	41

ALT = alanine aminotransferase; CFU = colony-forming units; NOAEL = no-observed-adverse-effect level; OECD = Organisation for Economic Co-operation and Development; TG = test guidelines

*It should be noted that the test articles evaluated in these studies may not be identical to the wINCI ingredients reviewed in this report; however, as they may be similar, both test articles and potentially related wINCI ingredients have been included in the table

**unknown if test substance is a cosmetic ingredient (e.g., *Candida oleophila* strain O); however, ingredient relates to INCI ingredient reviewed in this report (Yeast Extract (when derived from *Candida oleophila*)

Table 12. Genotoxicity studies*

Ingredient	Test Article	Vehicle	Concentration/Dose	Test System	Procedure	Results	Reference
			IN VITRO				
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate**	sterile water	10, 50, 100, 500, 1000, 2500, 5000, and 10,000 µg/plate	*S. typhimurium strains* TA98, TA100, TA1538, and TA1535*; E. coli* WP2 urvA	Ames assay; performed with and without metabolic activation; vehicle used as negative control; positive controls: AF-2, ENNG, 9-AA, and 2-NF	Non-genotoxic; controls gave expected results	[48]
Hydrolyzed Saccharomyces Cell Wall	90% yeast (*Saccharomyces cerevisiae*) cell wall (containing 24% glucan and 7% mannan)**	HSCAS	3.4, 10.3, 30.98, 92.6, 277.8, 833.3, and 2500 µg/plate	*S. typhimurium* strains TA1535, TA1537, TA98, and TA102	Ames assay; OECD TG 471; performed with and without metabolic activation; vehicle used as negative control; positive controls: sodium azide, 9-aminoacridine, 2-nitro fluorene, mitomycin C, 2-anthramine, and benzo[a]pyrene	Non-genotoxic; controls gave expected results	[4]
Phaffia Rhodozyma Extract and Phaffia Rhodozyma Ferment Extract	*Phaffia rhodozyma* extract**	acetone	25 µl; 1.22 – 5000 µg/ plate	*S. typhimurium* strains TA 98 and TA100	Ames assay; OECD TG 471; performed with and without metabolic activation; vehicle used as negative control; positive controls: AF-2 and 2-AA	Non-genotoxic; controls gave expected results	[45]
Phaffia Rhodozyma Extract and Phaffia Rhodozyma Ferment Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	sterile water	1.5, 5, 15, 50, 150, 500, 1500, and 5000 µg/plate	*S. typhimurium* strains TA98, TA100, TA1537, and TA1535*; E. coli* WP2 *urvA*	Ames assay; OECD TG 471; performed with and without metabolic activation; vehicle used as negative control; positive controls: 2-AA and 2-NF, sodium azide, 2-aminoacridine, methylmethanesulfonate	Non-mutagenic; controls gave expected results	[46]
Pichia Minuta Extract	Pichia Minuta Extract	NR	At least 5 concentrations tested	4 strains of *S. typhimurium*; one strain of *E. coli* (specific strains not stated)	Ames assay; OECD TG 471	Non-mutagenic	[39]
Pichia Minuta Extract	Pichia Minuta Extract	NR	NR	TK6 lymphoblastoid human cells	micronucleus assay	Non-mutagenic	[39]
Saccharomyces Ferment	fermentate powder derived from *Saccharomyces cerevisiae***	methylcellulose and water	5, 10, 50, 100, 500, 1000, 2500, and 5000 µg/plate	*S. typhimurium* strains TA97a, TA98, TA100, and TA1535; *E. coli* WP2 *urvA*	Ames assay; OECD TG 471; performed with and without metabolic activation; negative control: sterile water	Non-genotoxic; controls gave expected results	[41]
Saccharomyces Ferment	fermentate powder derived from *Saccharomyces cerevisiae***	methylcellulose and water	up to 5000 µg/ml (specific concentrations tested not stated)	mouse lymphoma L5178Y cell line	mammalian cell gene mutation assay; OECD TG 476; positive controls: methyl methanesulfonate and cyclophosphamide	Non-genotoxic; controls gave expected results	[41]
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	sterile water	1.5, 5, 15, 50, 150, 500, 1500, and 5000 µg/plate	*S. typhimurium* strains TA98, TA100, TA1537, and TA1535*; E. coli* WP2 *urvA*	Ames assay; OECD TG 471; performed with and without metabolic activation; vehicle used as negative control; positive controls: 2-AA and 2-NF, sodium azide, 2-aminoacridine, methylmethanesulfonate	Non-mutagenic; controls gave expected results	[47]
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* strain O**	NR	at least 5 concentrations tested	4 strains of *S. typhimurium*; one strain of *E. coli* (specific strains not stated)	Ames assay performed with and without metabolic activation; OPPTS Guideline 870.5100	Non-mutagenic	[42]
Yeast Extract (when derived from *Candida oleophila*)	*Candida oleophila* strain O**	NR	at least 4 concentrations tested	NR	mammalian cell gene mutation assay performed with and without metabolic activation; OPPTS Guideline 870.5300	Non-mutagenic	[42]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract (derived from *Pichia naganishii*)	NR	at least 5 concentrations tested	4 strains of *S. typhimurium*; one strain of *E. coli* (specific strains not stated)	Ames assay; OECD TG 471	Non-mutagenic	[39]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract (derived from *Pichia naganishii*)	NR	NR	L5178Y TK+/- mouse lymphoma cells	micronucleus assay	Non-mutagenic	[39]

Table 12. Genotoxicity studies*

Ingredient	Test Article	Vehicle	Concentration/Dose	Test System	Procedure	Results	Reference
			IN VIVO				
Phaffia Rhodozyma Extract and Phaffia Rhodozyma Ferment Extract	*Phaffia rhodozyma* extract**	corn oil	500, 1000, and 2000 mg/kg bw/d	male ICR mice (3/group)	mammalian bone marrow chromosomal aberration assay; OECD TG 475; negative control group received corn oil orally (method of oral administration not stated); once a day treatment for 2 d; positive control group received injection of mitomycin C	Non-clastogenic; controls gave expected results	45
Hydrolyzed Saccharomyces Cell Wall	90% yeast (*Saccharomyces cerevisiae*) cell wall (containing 24% glucan and 7% mannan)**	HSCAS	500, 1000, and 2000 mg/kg bw/d	Swiss ICO OF1 mice (28/sex/group)	mammalian bone marrow chromosomal aberration assay; OECD TG 475; gavage administration; once a day treatment for 2 d; negative control: 0.5% methylcellulose in purified water; positive control group: cyclophosphamide in 0.9% saline	Non-clastogenic; controls gave expected results	4

2-AA = 2-aminoanthracene; 2-NF = 2-nitrofluorene; 9-AA = 9-aminoadridine; AF-2 = 2-(2-furyl)-3-(5-nitro-2-furyl) acrylamide; ENNG = 1-ethyl-2-nitro-3-nitrosguanidine; NR = not reported; OECD TG = Organisation for Economic Co-operation and Development test guidelines; OPPTS = Office of Prevention, Pesticides, and Toxic Substances

*It should be noted that the test articles evaluated in these studies may not be identical to the wINCI ingredients reviewed in this report; however, as they may be similar, both test articles and potentially related wINCI ingredients have been included in the table

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
			IRRITATION			
			In Vitro			
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)	trade name mixture containing Hydrolyzed Saccharomyces Cell Wall (8-10%), phenoxyethanthol (0.5%), lactic acid (0.16 – 0.22%), alcohol (4%), fragrance (< 0.1%), and water (residual)	100%; 25 µl	reconstructed human epidermis model	LabCyte EPI-MODEL24 SIT; OECD TG 439; negative control of water; positive control of sodium dodecyl sulfate; 15 min application time	non-irritating	13
Phaffia Rhodozyma Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	65
Saccharomyces Cerevisiae Extract	powdered *Saccharomyces cerevisiae* extract****	tested neat; 10 mg moistened with 5 µl water	human three-dimensional epidermal model (EpiSkin™)	human epidermis model; negative control of PBS; positive control of sodium dodecyl sulfate; 15 min exposure followed by 42-h recovery period; colorimetric measurement of MTT reduction was used as index of cell viability	non-irritating	2
Saccharomyces Cerevisiae Extract	trade name mixture containing 1.25% Saccharomyces Cerevisiae Extract	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	66

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Saccharomyces Cerevisiae Extract	trade name mixture containing 3% Saccharomyces Cerevisiae Extract	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	69
Saccharomyces Cerevisiae Extract	trade name mixture containing 4.5% Saccharomyces Cerevisiae Extract	25, 50, 75, 100, and 135 µl	Irritection® system**	Test substance applied to membrane for 24 h; irritancy measured via a spectrophotometer	non-irritating	64
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	67
Saccharomyces Lysate Extract	trade name mixture containing 10% Saccharomyces Lysate Extract	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	70
Saccharomyces Lysate Extract	trade name mixture containing 98% Saccharomyces Lysate Extract	tested neat; 30 µl	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ assay; 3 tissue inserts incubated with test substance for 60 min, followed by washing, re-plating, and MTT assay; negative control of PBS; positive control of sodium dodecyl sulfate	non-irritating	68
Animal						
Hydrolyzed Saccharomyces Cell Wall	mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall (24% glucan and 7% mannan) in 10% HSCAS****	55%; moistened with distilled water	3 male New Zealand albino rabbits	Test substance mixture (0.91 g) was placed on gauze pad and applied to one 6 cm^2 dose site on each animal. The pad was wrapped under semi-occlusive conditions. Pads were kept on for 4 h. Erythema and edema were evaluated 30 - 60 min, 24, 48, and 72 h after patch removal. Sites were scored according to the Draize scoring system.	Slight erythema noted within 30 - 60 min after dressing removal; primary dermal irritation of 0.1; classified as slightly irritating	4
Yeast Extract (when derived from *Candida oleophila*)	non-cosmetic product containing *Candida oleophila* strain O (as an active ingredient at 57% by weight)****	100%; 0.5 g	3 rabbits (sex and strain not stated)	primary dermal irritation study; application to 25 mm x 25 mm area for 4 h; level of occlusion not stated; animals observed for 72 h; irritation scored by Draize method	non-irritating; primary irritation index: 0	42
Human						
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate****	100%	45 subjects	continuous skin irritation test; gauze (10 cm^2) containing test substance applied to cheek for 15 min, once per day, for 40 d; level of occlusion not stated	No adverse reactions observed.	71
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)	trade name mixture containing Hydrolyzed Saccharomyces Cell Wall (8-10%), phenoxyethanol (0.5%), lactic acid (0.16 – 0.22%), alcohol (4%), fragrance (< 0.1%), and water (residual)	100%	20 subjects	24-h patch test; occlusive conditions; sites evaluated 60 min and 24 h after patch removal	non-irritating	13
Lipomyces Lipid Bodies and Lipomyces Oil	cream consisting of 100% Lipomyces Lipid Bodies***	100%	NR	4-wk dermal exposure; subjects used cream on face and hands for an average period of 27.6 d	The test substance was considered to be well-tolerated	25
Metschnikowia Agaves Extract	Metschnikowia Agaves Extract	15% in water	11 subjects	patch test; no other details provided	non-irritating	20
Pichia Anomala Extract	Pichia Anomala Extract	15% in water	10 subjects	patch test; no other details provided	non-irritating	20
Pichia Anomala Extract	Pichia Anomala Extract	15% in water	10 subjects	patch test; no other details provided	non-irritating	20

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Pichia Heedii Extract	Pichia Heedii Extract	15% in water	10 subjects	patch test; no other details provided	non-irritating	[20]
Pichia Minuta Extract	Pichia Minuta Extract	15% in water	11 subjects	patch test; no other details provided	non-irritating	[20]
Saccharomyces Cerevisiae Extract	cosmetic formulation containing 1% Saccharomyces Cerevisiae Extract	tested neat	28 subjects	20 µl were applied to the skin, under an occlusive patch, for 48 h; skin irritation was evaluated for irritation 15 min and 48 h after patch removal	Slight erythema noted in one volunteer 15 min after patch removal; however, no reaction was noted 48 h after patch removal	[72]
Yeast Extract	Yeast Extract derived from *Candida magnoliae*	15% in water	10 subjects	patch test; no other details provided	non-irritating	[20]
Yeast Extract (may also be chemically similar to Hydrolyzed Candida Saitoana Extract)	Yeast Extract derived from *Candida saitoana*	15% in water	10 subjects	patch test; no other details provided	non-irritating	[20]
Yeast Extract derived from *Metschnikowia pulcherrima*	Yeast Extract derived from *Metschnikowia pulcherrima*	15% in water	10 subjects	patch test; no other details provided	non-irritating	[20]
Yeast Extract (may also be chemically similar to Hydrolyzed Metschnikowia Reukaufii Extract)	Yeast Extract derived from *Metschnikowia reukaufii*	15% in water	11 subjects	patch test; no other details provided	non-irritating	[20]
SENSITIZATION						
In Chemico/In Vitro						
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)	trade name mixture containing Hydrolyzed Saccharomyces Cell Wall (8-10%), phenoxyethanol (0.5%), lactic acid (0.16 – 0.22%), alcohol (4%), fragrance (< 0.1%), and water (residual)	up to 400 µg	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[13]
Hydrolyzed Yeast	trade name mixture containing 0.4% Hydrolyzed Yeast, 30% 1,3-butylene glycol, 0.08% polysorbate 20, and 69.52% water)	up to 2000 µM	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[75]
Hydrolyzed Yeast	trade name mixture containing 0.4% Hydrolyzed Yeast, 30% 1,3-butylene glycol, 0.08% polysorbate 20, and 69.52% water)	up to 5000 µg/ml	THP-1 cell line	h-CLAT; OECD TG 442E	no sensitization potential	[75]
Phaffia Rhodozyma Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	100 mM in acetonitrile	lysine and cysteine peptides	DPRA; OECD TG 442C	no sensitization potential	[73]
Phaffia Rhodozyma Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	up to 2000 µM	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[76]
Pichia Minuta Extract	Pichia Minuta Extract	NR	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[39]
Pichia Minuta Extract	Pichia Minuta Extract	NR	U937 cell line	U-SENS™; OECD TG 442E	no sensitization potential	[39]

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	100 mM in acetonitrile	Lysine and cysteine peptides	DPRA; OECD TG 442C	no sensitization potential	[74]
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	up to 2000 µM	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[74]
Yeast Extract (when derived from *Candida magnoliae)*	Yeast Extract (derived from *Candida magnoliae)*	NR	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[39]
Yeast Extract (may also be chemically similar to Hydrolyzed Metschnikowia Reukaufii Extract)	Yeast Extract derived from *Metschnikowia reukaufii*	100%	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[20]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract (derived from *Pichia naganishii*)	NR	KeratinoSens™ cell line	ARE-Nrf2 Luciferase Test; OECD TG 442D	no sensitization potential	[39]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract (derived from *Pichia naganishii*)	NR	THP-1 cell line	h-CLAT; OECD TG 442E	no sensitization potential	[39]
			Animal			
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate****	100%	10 female Hartley guinea pigs/group	Guinea pig maximization assay: intradermal induction: 3 pairs of injections on day 1: 1.) adjuvant + distilled water 2.) test article 3.) test article + adjuvant/distilled water topical induction: 48-h occlusive patch (2 x 4 cm patch) on day 7 challenge: 24-h occlusive patch (20 mm x 20 mm) on day 21	0% sensitization rate	[77]
Hydrolyzed Saccharomyces Cell Wall (*derived from Saccharomyces cerevisiae*)	mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall (24% glucan and 7% mannan) in 10% HSCAS****	55%; vehicle of 2% carboxymethylcellulose in distilled water	male Hartley guinea pigs (20 test group, 10 control group)	Buehler test; OECD TG 406; Once each week for 3 wk, the test substance was applied to the animal's left side under an occlusive patch and left on for 6 h. Readings were made 24 and 48 h after each induction period. Twenty-seven days after the first induction dose, the test substance was applied, under an occlusive patch, on a naïve site on the right side of the animal as a challenge dose. Sites were evaluated for a sensitization response 24 and 48 h after challenge application. A control group was treated with HSCAS, only.	non-irritating; non-sensitizing	[4]
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract****	0, 10, 25, and 50% in propylene glycol	female CBA/J mice (5/group)	LLNA; OECD TG 429; The dorsal surface of both ears were epidermally treated (25 µl/ear) with the test substance, once a day for 3 d. Control animals were treated with the vehicle only. On day 6, animals were injected via the tail vein with 0.25 ml PBS containing 3H-methyl thymidine, and 5 h later ,killed. The auricular lymph node was excised, evaluated, and drained. Radioactivity measurements were performed. The SI was evaluated for each group. The SI is the ratio of the dpm/group compared to dpm/vehicle control group. An SI ≥ 3 indicates potential skin sensitization.	SI values at the 10, 25, and 50% concentration levels were 2.1, 5, and 28.9, respectively. The estimated test substance concentration that would give an SI = 3 was calculated to be 14.7%. The test substance was considered to be sensitizing.	[2]

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract****	0, 10, 25, and 50% in propylene glycol	female CBA/J mice (5/group)	LLNA performed according to the same procedure as above	SI values at the 10, 25, and 50% concentration levels were 1.1, 2, and 1.7, respectively. The test substance was considered to be non-sensitizing.	[2]
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract****	0, 10, 25, and 50% in propylene glycol	female CBA/J mice (5/group)	LLNA performed according to the same procedure as above	SI values at the 10, 25, and 50% concentration levels were 2.5, 2.5, and 1.8, respectively. The test substance was considered to be non-sensitizing.	[2]
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract****	0, 10, 25, and 50% in propylene glycol	female CBA/J mice (5/group)	LLNA performed according to the same procedure as above	SI values at the 10, 25, and 50% concentration levels were 1.4, 1.7, and 2.6, respectively. The test substance was considered to be non-sensitizing.	[2]
Saccharomyces Cerevisiae Extract	*Saccharomyces cerevisiae* extract**	0, 2.5, 5, 10, 25, and 50% in acetone and olive oil	female CBA mice (4/group)	LLNA performed according to the same procedure as above	SI values at the 2.5, 5, 10, 25, and 50% concentration levels were 0.87, 0.49, 1.36, 0.71, and 0.63, respectively. The test substance was considered to be non-sensitizing.	[2]
Human						
Galactomyces Ferment Filtrate	skincare product containing 1.485% Galactomyces Ferment Filtrate	100%	104 subjects	HRIPT; semi-occlusive conditions (patch size 8 mm); 9 induction patches; challenge patch applied 10-14 d after last induction patch	non-irritating and non-sensitizing	[79]
Galactomyces Ferment Filtrate	facial treatment essence containing 92.675% Galactomyces Ferment Filtrate	100%	100 subjects	HRIPT; occlusive conditions (patch size: 4 cm^2); 9 induction patches; challenge patch applied 12-20 d after last induction patch	non-sensitizing	[84]
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)	trade name mixture containing Hydrolyzed Saccharomyces Cell Wall (8-10%), phenoxyethanol (0.5%), lactic acid (0.16 – 0.22%), alcohol (4%), fragrance (< 0.1%), and water (residual)	100%	50 subjects	HRIPT; level of occlusion and patch size not stated; 9 induction patches; challenge patch applied 2 wk after last induction patch	non-irritating and non-sensitizing	[13]
Hydrolyzed Yeast	trade name mixture containing 0.4% Hydrolyzed Yeast, 30% 1,3-butylene glycol, 0.08% polysorbate 20, and 69.52% water	0.01%	51 subjects	HRIPT; occlusive condition (patch size: 4 cm^2); 9 induction patches; challenge patch applied 2 wk after last induction patch	non-irritating and non-sensitizing	[80]
Metschnikowia Agaves Extract	Metschnikowia Agaves Extract	15% in water	112 subjects	HRIPT; no other details provided	non-sensitizing	[20]
Pichia Anomala Extract	Pichia Anomala Extract	15% in water	104 subjects	HRIPT; no other details provided	non-sensitizing	[20]
Pichia Anomala Extract	Pichia Anomala Extract	15% in water	100 subjects	HRIPT; no other details provided	non-irritating; non-sensitizing	[20]
Pichia Heedii Extract	Pichia Heedii Extract	15% in water	106 subjects	HRIPT; no other details provided	non-irritating; non-sensitizing	[20]
Pichia Minuta Extract	Pichia Minuta Extract	15% in water	107 subjects	HRIPT; no other details provided	non-sensitizing	[20]

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
Saccharomyces Ferment Lysate Filtrate	cream containing 0.0135% Saccharomyces Ferment Lysate Filtrate	100%	52 subjects	HRIPT; occlusive conditions (patch size: 2 cm^2); 9 induction patches; challenge patch applied 2 wk after last induction patch	non-irritating and non-sensitizing	[81]
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 2% Saccharomyces Ferment Lysate Filtrate non-volatile solids in water	100%	105 subjects	HRIPT; semi-occlusive conditions (patch size 8 mm^2); 9 induction patches; challenge patch applied 10 - 14 d after last induction patch	non-irritating and non-sensitizing	[83]
Saccharomyces Lysate Extract	cream containing 0.028% Saccharomyces Lysate Extract	100%	50 subjects	HRIPT; occlusive conditions (patch size: 2 cm^2); 9 induction patches; challenge patch applied 2 wk after last induction patch	non-irritating and non-sensitizing	[78]
Saccharomyces Lysate Extract	trade name mixture containing 25% Saccharomyces Lysate Extract	10% in water	50 subjects	open patch repeat patch test; 0.2 ml applied to back per application and allowed to air dry; 9 induction patches; challenge patch 10 - 14 d after last induction patch	non-irritating and non-sensitizing	[85]
Yeast Extract	lotion containing 0.0045% Yeast Extract	100%	52 subjects	HRIPT; occlusive conditions (patch size: 2 cm^2); 9 induction patches; challenge patch applied 2 wk after last induction patch	non-irritating and non-sensitizing	[82]
Yeast Extract (may also be chemically similar to Hydrolyzed Candida Saitoana Extract)	Yeast Extract derived from *Candida saitoana*	15% in water	112 subjects	HRIPT; no other details provided	non-sensitizing	[20]
Yeast Extract (may also be chemically similar to Hydrolyzed Metschnikowia Reukaufii Extract)	Yeast Extract derived from *Metschnikowia reukaufii*	15% in water	104 subjects	HRIPT; no other details provided	non-sensitizing	[20]
PHOTOTOXICITY						
In Vitro						
Phaffia Rhodozyma Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	0.5, 1.5, 5, and 10%	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ phototoxicity assay; incubated tissue inserts irradiated with UVA for 60 min (6 J/cm^2); controls not exposed to UVA; cell viability measured via MTT assay; chloropromazine used for positive control	predicted to be non-phototoxic	[86]
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	0.5, 1.5, 5, and 10%	reconstructed human epidermal model (EpiDerm™)	EpiDerm™ phototoxicity assay; incubated tissue inserts irradiated with UVA for 60 min (6 J/cm^2); controls not exposed to UVA; cell viability measured via MTT assay; chloropromazine used for positive control	predicted to be non-phototoxic	[87]
Animal						
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate****	100%	3 male New Zealand white rabbits	Test material (0.8 ml) applied to shaved skin under 4 cm^2 flannel cloth lined with surgical tape for 24 h (level of occlusion not stated); irradiation with long-wavelength ultraviolet rays (1.2 x 10^8 erg/cm^2) for 3 h; observations performed 24 and 48 h after irradiation	non-phototoxic	[89]

Table 13. Dermal irritation and sensitization studies*

Ingredient	Test Article	Concentration/Dose	Test Population	Procedure	Results	Reference
PHOTOSENSITIZATION						
Animal						
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate****	100%	female Hartley albino guinea pigs (10/group)	Guinea pig photosensitization assay: 1) animals injected with adjuvant 2) 20% aqueous solution of sodium lauryl sulfate applied, 24 h later, cellophane tape adhered and removed 7 times 3) test material (0.4) applied, animals irradiated with long-wavelength ultraviolet rays (1.2×10^8 erg/cm^2) for 3 h Steps 2 and 3 were repeated 5 times every other day. For the challenge test, on the 4th week of the study, 0.8 ml of the test substance was applied to the back, and animals were irradiated for 1 h; potential photosensitization observed 24 and 48 h after treatment	non-photosensitizing	[88]

ARE = antioxidant response element; dpm = disintegrations per minute; DPRA = direct peptide reactivity assay; h-CLAT = human cell line activation test; HSCAS = hydrated sodium calcium aluminosilicate; HRIPT = human repeat insult patch test; LLNA = local lymph node assay; MTT = 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide; Nrf2 = nuclear factor erythroid 2-related factor 2; OECD = Organisation for Economic Co-operation and Development; PBS = phosphate-buffered saline; SI = stimulation index; TG = test guideline; THP-1 = human monocytic cell line; U-SENS = U937 cell line activation test; UVA = ultraviolet A

*It should be noted that the test articles evaluated in these studies may not be identical to the wINCI ingredients reviewed in this report; however, as they may be similar, both test articles and potentially related wINCI ingredients have been included in the table

**the Irritection® system involved the use of a proprietary solution comprised of both proteins and macromolecules in a well that is covered by a membrane. The test material is applied to the membrane and diffuses into the well. The proteins and macromolecules within the well undergo conformational changes depending on the irritation potential of the test substance that mimic the biomolecular changes that occur when irritants are placed on the skin and eyes. The more turbid the solution becomes, the higher the irritancy level. Irritancy is measured using a spectrophotometer.

***Lipomyces Lipid Bodies naturally contain 87% Lipomyces Oil per lipid body

****unknown if test substance is a cosmetic ingredient (e.g., *Candida oleophila* strain O); however, ingredient relates to INCI ingredient reviewed in this report (Yeast Extract (when derived from *Candida oleophila*)

Table 14. Sensitization data profile per ingredient, identifying those assessing AOP key events, animal studies, and human studies

Ingredient	Key Event 1	Key Event 2	Key Event 3	Key Event 4	GPMT/Buehler	HRIPT
Galactomyces Ferment Filtrate					GPMT	HRIPT
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces cerevisiae*)					Buehler	
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)		KeratinoSens™				HRIPT
Hydrolyzed Yeast		KeratinoSens™	h-CLAT			HRIPT
Metschnikowia Agaves Extract						HRIPT
Phaffia Rhodozyma Extract	DPRA	KeratinoSens™				
Pichia Anomala Extract						HRIPT
Pichia Heedii Extract						HRIPT
Pichia Minuta Extract		KeratinoSens™	U-SENS			HRIPT
Saccharomyces Cerevisiae Extract				LLNA		
Saccharomyces Ferment Lysate Filtrate	DPRA	KeratinoSens™				HRIPT
Saccharomyces Lysate Extract						HRIPT
Yeast Extract						HRIPT
Yeast Extract (derived from *Candida magnoliae*)		KeratinoSens™				
Yeast Extract (derived from *Candida saitoana*)						HRIPT
Yeast Extract (derived from *Metschnikowia reukaufii*)		KeratinoSens™				HRIPT
Yeast Extract (derived from *Pichia naganishii*)		KeratinoSens™	h-CLAT			

DPRA = direct peptide reactivity assay; GPMT = guinea pig maximization test; h-CLAT = human cell line activation test; HRIPT = human repeated insult patch test; U-SENS = U937 cell line activation test

Table 15. Ocular irritation studies

Ingredient	Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
				IN VITRO			
Galactomyces Ferment Filtrate	facial treatment essence containing 92.675% *Galactomyces* ferment filtrate	NR	100%	human cell construct model (EpiOcular™)	tissue equivalent assay with EpiOcular™ cultures; MTT assay used to evaluate cellular metabolism after exposure to test article for various exposure times (10, 30, 60, and 180 min); sterile deionized water used as negative control; octoxynol-9 used as positive control	non-irritating; definitive t_{50} determined to be >240; controls gave expected results in definitive assay	90
Hydrolyzed Saccharomyces Cell Wall (derived from *Saccharomyces pastorianus*)	trade name mixture containing Hydrolyzed Saccharomyces Cell Wall (8-10%), phenoxyethanol (0.5%), lactic acid (0.16 – 0.22%), alcohol (4%), fragrance (< 0.1%), and water (residual)	NR	100%; 50 µl	human corneal epithelial cells	LabCyte CORNEA-MODEL24 EIT; OECD TG 492; phosphate-buffered saline used as negative control; ethanol used as positive control; 1 min exposure period	non-irritating; controls gave expected results	13
Phaffia Rhodozyma Extract	trade name mixture containing 49% Phaffia Rhodozyma Extract	NR	100%	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; 30 min incubation; MTT assay performed; sterile deionized water used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	65

Table 15. Ocular irritation studies

Ingredient	Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
Pichia Minuta Extract	Pichia Minuta Extract	NR	NR	bovine eyes	bovine corneal opacity and permeability test method; OECD TG 437	Test substance did not require classification of eye irritation or serious eye damage	[39]
Saccharomyces Cerevisiae Extract	trade name mixture containing 1.25% Saccharomyces Cerevisiae Extract	NR	100%: 50 µl	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; tissues treated and incubated for 90 min; PBS used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	[66]
Saccharomyces Cerevisiae Extract	trade name mixture containing 3% Saccharomyces Cerevisiae Extract	NR	100%	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; 30 min incubation; MTT assay performed; sterile deionized water used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	[69]
Saccharomyces Cerevisiae Extract	trade name mixture containing 4.5% Saccharomyces Cerevisiae Extract	NR	25, 50, 75, 100, and 125 µl	Irritection® systems	Irritection® assay*	Test substance was considered to be minimally irritating at all tested concentrations (all scores under 12.5 are considered to be minimally irritating). Irritation scores resulting from doses of 25, 50, 75, 100, and 125 µl were 5.2, 5.5., 6.1, 6.4, and 7.2, respectively.	[64]
Saccharomyces Cerevisiae Extract	powdered *Saccharomyces cerevisiae* extract***	physiological saline	20%; 750 µl	bovine corneas	bovine corneal opacity and permeability test; OECD TG 437; negative control: physiological saline; positive control: 20% imidazole	Test substance not considered to be severe irritant or corrosive. Mean irritation score of test substance: 3.3 Mean irritation score of negative control: below upper limits of laboratory historical range Mean irritation score of positive control: 119	[2]
Saccharomyces Ferment Lysate Filtrate	trade name mixture containing 24.5% Saccharomyces Ferment Lysate Filtrate	NR	100%	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; 30 min incubation; MTT assay performed; sterile deionized water used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	[67]
Saccharomyces Lysate Extract	trade name mixture containing 98% Saccharomyces Lysate Extract	NR	100%	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; 30 min incubation; MTT assay performed; sterile deionized water used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	[68]
Saccharomyces Lysate Extract	trade name mixture containing 10% Saccharomyces Lysate Extract	NR	100%	corneal epithelial model (EpiOcular™)	EpiOcular™ assay; 30 min incubation; MTT assay performed; sterile deionized water used as negative control; methyl acetate used as positive control	non-irritating; controls gave expected results	[70]
Yeast Extract (when derived from *Pichia naganishii*)	Yeast Extract derived from *Pichia naganishii*)	NR	NR	bovine eyes	bovine corneal opacity and permeability test method; OECD TG 437	test substance did not require classification of eye irritation or serious eye damage	[39]

Table 15. Ocular irritation studies

Ingredient	Test Article	Vehicle	Concentration/Dose	Test Population	Procedure	Results	Reference
				ANIMAL			
Galactomyces Ferment Filtrate	*Galactomyces* ferment filtrate***	NR	0.1 ml (concentration not stated)	3 Japanese white rabbits (sex not stated)	test substance instilled in right eye; control substance instilled in left eye (control substance used not stated); eyes evaluated immediately after, 3, 6, 24, 48, and 72 h after administration	non-irritating	[91]
Hydrolyzed Saccharomyces Cell Wall (when derived from *Saccharomyces cerevisiae*)	mixture containing 90% yeast (*Saccharomyces cerevisiae*) cell wall*****	HSCAS	100%; 0.09 g	3 male New Zealand albino rabbits	One eye of each animal anesthetized and test substance instilled into conjunctival sac; irritation evaluated using high-intensity white light at 1, 24, 48, and 72 h post-instillation	mildly irritating; no corneal opacity or iritis was observed in any treated eye during the study. One hour following test substance administration, all treated eyes exhibited positive conjunctivitis. The severity of irritation decreased with time, with no irritation noted 72 h after instillation.	[4]
Saccharomyces Cerevisiae Extract	powdered *Saccharomyces cerevisiae* extract***	NR	100%; 59 mg	3 male New Zealand White rabbits	test substance placed in one eye of each rabbits; examination 1, 24, 48, and 72 h after instillation; 24 h after instillation, 2% fluorescein in water solution instilled to evaluate epithelial damage	Irritation of the conjunctivae, presenting as redness, chemosis, and discharge, was noted in treated eyes; however, this irritation was completely resolved within 48 h for all animals.	[2]
Yeast Extract (when derived from *Candida oleophila*)	non-cosmetic product containing *Candida oleophila* strain O (as an active ingredient at 57% by weight)***	NR	100%; 100 mg	4 rabbits (sex and strain not stated)	test substance instilled in conjunctive sac of the right eye; animals observed for 15 d	minimally irritating	[42]

HSCAS = hydrated sodium calcium aluminosilicate; OECD = Organisation for Economic Co-operation and Development test guidelines; PBS = phosphate-buffered saline; t_{50}= duration of exposure resulting in a 50% decrease in MTT conversion; TG = test guideline

*the Irritection® system involved the use of a proprietary solution comprised of both proteins and macromolecules in a well that is covered by a membrane. The test material is applied to the membrane and diffuses into the well. The proteins and macromolecules within the well undergo conformational changes depending on the irritation potential of the test substance that mimic the biomolecular changes that occur when irritants are placed on the skin and eyes. The more turbid the solution becomes, the higher the irritancy level. Irritancy is measured using a spectrophotometer.
**_Saccharomyces cerevisiae_ cell wall contains 24% glucan and 7% mannan
***unknown if test substance is a cosmetic ingredient (e.g., *Candida oleophila* strain O); however, ingredient relates to INCI ingredient reviewed in this report (Yeast Extract (when derived from *Candida oleophila*)

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