Safety Assessment of Soy-Derived Ingredients as Used in Cosmetics

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All interested persons are provided 60 days from the above release date to comment on this safety assessment and to identify additional published data that should be included or provide unpublished data which can be made public and included.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 All unpublished data submitted to CIR will be discussed in open meetings, will be available at the CIR office for review by any interested party and may be cited in a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.

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

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INTRODUCTION

This scientific literature review is the initial step in preparing a safety assessment of the following 28 soy-derived ingredients as used in cosmetic formulations:

Glycine Max (Soybean) Callus Culture
Glycine Max (Soybean) Callus Culture Extract
Glycine Max (Soybean) Callus Extract
Glycine Max (Soybean) Fiber
Glycine Max (Soybean) Flower/Leaf/Stem Juice
Glycine Max (Soybean) Leaf Cell Extract
Glycine Max (Soybean) Leaf Extract
Glycine Max (Soybean) Phytoplacenta Conditioned Media
Glycine Max (Soybean) Phytoplacenta Extract
Glycine Max (Soybean) Pulp
Glycine Max (Soybean) Seed Extract
Glycine Max (Soybean) Seedcake Extract
Glycine Max (Soybean) Seedcoat Extract
Glycine Max (Soybean) Seed Powder
Glycine Max (Soybean) Sprout Extract
Glycine Soja (Soybean) Extract
Glycine Soja (Soybean) Fiber
Glycine Soja (Soybean) Flour
Glycine Soja (Soybean) Germ Extract
Glycine Soja (Soybean) Hull
Glycine Soja (Soybean) Lipids
Glycine Soja (Soybean) Phytoplacenta Extract
Glycine Soja (Soybean) Seed
Glycine Soja (Soybean) Seedcake Extract
Glycine Soja (Soybean) Seed Extract
Glycine Soja (Soybean) Seed Powder
Glycine Soja (Soybean) Seed Water
Glycine Soja (Soybean) Sprout Extract

According to the web-based *International Cosmetic Ingredient Dictionary and Handbook (*wINCI *Dictionary)*, the majority of these ingredients are reported to function as antioxidants, skin protectants, skin-conditioning agents – miscellaneous, and hair-conditioning agents; several other functions are also reported.[1] (Table 1)

Several soy-derived ingredients such as Glycine Soja (Soybean) Oil, Glycine Soja (Soybean) Sterols, Glycine Soja (Soybean) Peptide, Glycine Soja (Soybean) Polypeptide, and Glycine Soja (Soybean) Protein, have been reviewed by the Cosmetic Ingredient Review (CIR). The full reports on these ingredients can be accessed on the CIR website (https://www.cir-safety.org/ingredients); therefore, information regarding these ingredients will not be included in this report.

Some of the ingredients reviewed in this safety assessment may be consumed as food, and daily exposure from food use would result in much larger systemic exposures than those from use in cosmetic products. Although oral studies are included, the primary focus of the safety assessment of these ingredients as used in cosmetics is on the potential for effects from topical exposure.

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

Botanicals, such as soy-derived ingredients, may contain hundreds of constituents, some of which may have the potential to cause toxic effects. In this assessment, CIR is reviewing the potential toxicity of each of the botanical ingredients as a whole, complex mixture.

It is often not known how the substance being tested in a study compares to the cosmetic ingredient. In the report text, if it is known that the material being tested is a cosmetic ingredient, the INCI naming convention will be used (i.e., the names of cosmetic ingredients are capitalized, without italics). If it is not known that the test substance is the same as the cosmetic ingredient, the taxonomic naming conventions will be used (i.e. with genus and species name italicized).

CHEMISTRY

Definition

All ingredients reviewed in this report are derived from the soybean plant (*Glycine max*). *Glycine max* is the domesticated version of its wild progenitor *Glycine soja*.[2] According to the *Dictionary*, *Glycine soja* is the accepted scientific name for *Glycine max*. The definitions of the soy-derived ingredients included in this review are provided in Table 1.[1]

Plant Identification

Soybeans (*Glycine max* and *Glycine soja*) are a species of legume native to East Asia, from where they have spread to Europe and the Americas.[3] Soybean plant height varies greatly, ranging from 0.2 to 2 m. The leaves of the plant are trifoliate, and fall before seeds mature. The fruit is a hairy pod containing 2-4 seeds. Soybeans of both subgenera (*Glycine max* and *Glycine soja*) are found in various colors. Typical soybeans are different shades of yellow, brown, green, or black.[4]

Compositions of soybeans may vary depending on the seed coat color. Details regarding this variation in composition dependent on color is described in the Composition section of this report.

According to a study, differences in plant morphological characteristics are attributed between the two subgenera *Glycine max* and *Glycine soja*.[5] The wild soybean, *Glycine soja*, grows in the form of creepers with many lateral branches. These plants flower later than the cultivated soybean and produce small black seeds. *Glycine max* produces large yellow seeds, with a fragile pod. In addition, differences at the genomic level between *Glycine max* and *Glycine soja* have been reported. However, such delineation between these species names is far from ubiquitous and these differences are not expected to affect their role in cosmetics; and therefore, the terms "soy" and "soybean" are instead used throughout much of this report. According to the wINCI *Dictionary*, the accepted scientific name for *Glycine soja* is *Glycine max*.[1]

Physical and Chemical Properties

Data on the chemical and physical properties of soy-derived ingredients were not found in the published literature.

Method of Manufacture

The methods below are general to the processing of soy products, and it is unknown if they apply to cosmetic ingredient manufacture.

Glycine Max (Soybean) Leaf Extract

The production of a soy leaf extract involves leaf washing, grinding, freeze-drying, and extraction using a 30-fold volume of 80% ethanol for 4 hours at room temperature.[6] The extracted solution was collected, and a vacuum evaporator was used to remove the ethanol solvent in the supernatant.

Glycine Max (Soybean) Pulp

To produce a black soybean pulp, black soybeans were soaked in water in a 3:1 ratio for 8 hours.[7] Pulp was obtained after grinding and removing the milk with a muslin cloth, and then freeze-dried.

Glycine Max (Soybean) Seedcoat Extract

In order to make a black soybean seedcoat extract, the black soybean seedcoat was extracted with acidic water and ethanol, purified using absorbent resin, and powdered by spray-drying.[7]

Glycine max (soybean) seed powder extract

Although soybean seed powder extract is not among the ingredients reviewed in this report, information regarding this related ingredient has been included below, as it may be useful.

To obtain a soybean powder, soybean seeds were washed with water, then dried.[8] The dried samples were ground to obtain the powdered form. To produce methanolic and hydroalcoholic extracts of seed powder samples were extracted separately with methanol (100%, 50%) by cold maceration. Approximately 30 g of seed powder samples were extracted three times with 280 mL methanol for 3 hours in an electrical shaker at 40º C. The extracts were then filtered and evaporated. The hydroalcoholic extract was produced in a similar manner, using alcohol and water as the extraction agents. Another method to produce seed powder extract involves successive extraction with solvents in increasing order of their polarity (hexane, chloroform, ethyl acetate, ethanol, and water). First, powder materials are passed through a sieve. The sieved powder is then extracted in a Soxhlet apparatus for 16 hours. The extract is then evaporated to dryness in a rotary vacuum evaporator at 40º C. In a different study, in order to prepare an ethanolic extract of the black soybean, black bean seeds were dried and ground.[9] The resulting powder was placed into an Erlenmeyer flask and suspended in 500 mL of 99% ethanol. This process was repeated two times. The extracts were then pooled, filtered, and dried using a rotary evaporator.

Glycine Max (Soybean) Sprout Extract

According to a study, the production of black soybean) sprout extract begins with soaking of the beans in deionized water.[10] The beans are then germinated, harvested, dried, crushed, and extracted by ultra-sonification, filtered, and centrifuged to separate the components and collect the supernatant.

Glycine Soja (Soybean) Extract

An n-hexane soy extract was produced by extracting soybeans (25 g) twice at room temperature by shaking for 48 hours with 500 mL n-hexane.[11] The combined n-hexane extracts were then dried in a vacuum desiccator under reduced pressure and concentrated using a rotavapor at 40 ºC. According to the same study, similar procedures are used in order to prepare ethyl acetate and ethanol soybean extracts.

Glycine Soja (Soybean) Flour

Soybean flour has been reported to be produced by mechanically removing the hull of the soybean, followed by extraction of the oil with hexane.[12] The residual hexane is either removed by indirect heating followed by steam sparging in a desolventizer toaster or by direct contact with superheated hexane in a flash desolventizer. The desolventized soy is then heat-processed, ground, and segregated to the desired particle-size distribution according to product specifications.

Composition

Powder Extract

Soybeans contain many bioactive phytochemicals, such as phenolic acids, flavonoids, isoflavonoids, saponins, phytosterols, and sphingolipids.[13] In order to determine the composition of 24 different soybeans, soybean seeds were ground to a powder and extracted with 80% methanol. The results of this study can be viewed in Table 2. The majorities of the extracts were made up of carbohydrates (30. 16 g/100g), fats (19.94 g/100g), and protein (36.49 g/100g). The isoflavonoids present in soybeans and soybean extracts have shown capacity to bind estrogen receptors and to elicit estrogen-like effects.[14] In addition, these isoflavones have shown anti-carcinogenic potential. Genotoxicity has also been observed in cells treated with these isoflavones, however, these effects are inconsistent, and are only prevalent in in vitro studies.

Germ Extract

The isoflavone content of dry soybean germ extracts extracted from ethanol (60-70%), methanol (80%), or ethanol (60%), were evaluated. The isoflavone content of each of these extracts were reported to be 40%, 26%, and 30%, respectively.

Soybean Extract

The bioactive compounds in a black soybean ethanolic extract were studied using thin layer chromatography (TLC).[9] Flavanoids, alkaloids, saponins, tannins, triterpenoids, and glycosides were found. In a different study, the anthocyanins, saponins, and isflavones of a black soybean extract were examined.[15] Approximately 1.3 g anthocyanins as a polyphenol (tannin) were present per 100 g. Isoflavones were found in the following amounts: daidzin (25 mg/100 g), daidzein (92 mg/100 g), genistin (22 mg/100 g), genistein (51 mg/100 g), and glycitin (16 mg/100 g). In soybeans, isoflavones are strongly associated with proteins.[16] These isoflavones can be dissociated from soy-proteins using alcohol extraction which significantly diminishes the amount of bound-isoflavones.

According to high-performance liquid chromatography (HPLC), a n-hexane soy extract contained a total isoflavone concentration of 27 mg/25 g extract.[11] Among these isoflavones were 40% daidzin, 56% genistin, 2% daidzein, and 2% genistein. An ethyl acetate soy extract and ethanolic soy extract contained a total isoflavone concentration of 48 mg/25 g and 52 mg/25 g, respectively. In a different study, a black soybean extract contained 32.5 mg gallic acid equivalent/g polyphenolics, 5.7% protein, 80.4 g glucose/100 g, and 5.1% lipid.[17] The total phenolic acid content was 6652.2 µg/g, including gallic acid, protocatechuic acid, caffeic acid, chlorogenic acid, m-coumaric acid, ferulic acid, and sinapic acid. The total phytochemical content was 11,776.5 µg/g, including daidzein, genistein, glycitein, daidzin, genistin, glycitin, acetyldaidzin, acetylgenistin, acetylglycitin, malonyldaidzin, malonylgenistin, and malonylglycitin. Flavanols included epigallocatechin (3003.8 µg/g), epicatechin (635.8 µg/g), and epicatechin gallate (735.5 µg/g), and anthocyanins included cyanidin-3-*O*-glucoside (921.4 µg/g), peonidin-3-*O*-glucoside (113.6 µg/g), dephinidin-3-*O*-glucoside (50.9 µg/g), petunidin-3-*O*-glucoside (40.7 µg/g), and pelargonidin-3-*O*-glucoside (38.8).

Seedcoat (Hull)

Thirty-nine samples of soybean hulls from feed mills and soy processors throughout the United States (US) were collected to examine their chemical composition.[18] The mean values of nutrients and amino acids found in these samples can be seen in Table 3. Among the samples, on average, amounts of 39.18 and 33.32% were found of nitrogen-free extract and crude fiber, respectively. Soybeans vary in composition based on color and country of origin. Black soybeans have unique properties owing to its black hull.[19] The black hull contains polyphenols, such as anthocyanins, procyanidins, and catechins. According to a study, the chemical composition of soybean hulls is dependent upon the efficiency of the dehulling process.[20] The soybean hulls may contain variable amounts of cellulose (29 - 51%), hemicelluloses (10 - 25%), lignin (1 - 4%), pectins (4 - 8%), proteins (11 - 15%), and minor extractives.

Seedcoat (Hull) Extract

A comparison of the composition of soybeans differing in seed coat color was examined.[4] Soybeans of a light yellow, dark yellow, brown, and black color were ground to a flour and analyzed for chemical composition and isoflavone content. Flours were defatted using n-hexane as a solvent for lipid extraction. Lipid, protein, ash, crude fiber, and carbohydrate content were similar among all tested groups. The average amount of lipids, protein, ash, crude fiber, and carbohydrates were 19.05, 37.8, 4.2, 6.3, and 24.7 g/100 g, respectively. Isoflavone content was determined by HPLC. Soybean flour extracted from soybeans with a light yellow seed coat showed the highest isoflavone content (415.98 mg/100 g), while soybean flour extracted from soybeans with a dark yellow seed coat showed the lowest isoflavone content (220.88 mg/100 g). All samples showed significantly different levels of isoflavone glycosides. Malonyl genistin, for

example, was discovered in amounts of 7498, 95.23, 138.57, and 116.29 mg/100 g, in dark yellow, brown, light yellow, and black soybean samples, respectively.

Pulp

HPLC was used to determine the isoflavone content of a black soybean pulp.[7] The amounts of daidzin, daidzein, genistin, and genistein in the black soybean pulp were determined to be 2.85, 0.27, 1.85, and 0.51 mg/100 g, respectively.

Sprout

The variation of isoflavone content in 17 different types of yellow and green soybean sprouts was studied using HPLC.[21] Yellow soybean sprouts were produced in a dark room. For green soybeans sprouts, seeds were germinated in the dark and then transferred to a box under a yellow light source. Sprouts were separated into cotyledons, hypocotyls, and roots. The average isoflavone concentration in the cotyledon, hypocotyl, and root of the green sprouts was 2167, 1169, and 2399 µg/g, respectively. The average isoflavone concentration in the cotyledon, hypocotyl, and root of the yellow sprouts was 2538, 1132, and 2852 µg/g, respectively.

Leaf Extract/ Seed Extract

The phytochemical content of ethanolic leaf and seed extracts were evaluated.[22] The total phenol, flavonoid, beta carotene, and lycopene content in the ethanolic leaf extract was 1092, 877, 40, and 0.69 mg/100 g extract, respectively. The total phenol, flavonoid, beta carotene, lycopene, and ascorbic acid content in the ethanolic seed extract was 938, 274, 11, 10, and 1.3 mg/100 g extract, respectively. In a different study, the phytochemical content of a methanolic soybean leaf extract was studied via various chromatographic procedures.[23] Among the 16 phytochemicals found were 6 isoflavones (4,5,7-trihydroxyisoflavone-7-*O*-β-D-glucopyranoside, 7-dihydroxy-6-methoxyisoflavone, 4,7-dihydroxyisoflavone, 4,7-dihydroxyisoflavone-7-*O*-β-D-glucopyranoside, 5,7,4'-trihydroxyflavone, 3',4',5,7-tetrahydroxyflavone, and 3',4',5-trihydroxyflavone-7-*O*-β-D-glucopyranoside), 1 flavanol (3,4',5,7-tetrahydroxyflavonol), 2 pterocarpans (coumestrol and glyceofuran), 2 phytosterols (4-hydroxybenzoic acid and methyl-4-hydroxybenzoate), 2 phenolic compounds (soyasapogenol B and stigmasterol) and 1 sugar alcohol (D-mannitol).

USE

Cosmetic

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

In some cases, VCRP data were given under a non-INCI name. For example, Glycine Soja (Soybean) Flour is considered an INCI name, but Glycine Max (Soybean) Flour, is not. VCRP data were available for Glycine Max (Soybean) Flour, but not for Glycine Soja (Soybean) Flour; therefore these data are reported for Glycine Soja (Soybean) Flour, as these names are believed to be synonymous since the accepted scientific name for *Glycine soja* is *Glycine max*.

According to 2019 VCRP data, Glycine Max (Soybean) Seed Extract is reported to be used in 395 formulations, 273 of which are leave-on formulations, and Glycine Max (Soybean) Flour (synonymous with Glycine Soja (Soybean) Flour) is reported to be used in 66 formulations (Table 4).[24,25] All other in-use ingredients are reported to be used in 51 formulations or less. The results of the 2016 concentration of use survey conducted by the Council indicate Glycine Soja (Soybean) Seed Extract has the highest concentration of use; it is used at up to 2% in face and neck products. Ingredients that are not reported to be in use, according to VCRP and Council survey data, can be seen in Table 5.

Incidental ingestion of these soy-derived ingredients is possible as Glycine Max (Soybean) Seed Extract and Glycine Max (Soybean) Lipids are used in lipstick formulations. In addition, these ingredients are used in in products applied near the eye (at a maximum concentration of up to 0.09% Glycine Soja (Soybean) Lipids).

Additionally, some of the soy-derived ingredients are used in cosmetic sprays and could possibly be inhaled; for example, Glycine Soja (Soybean) Seed Extract is reported to be used at a concentration of 0.000001% in hair spray formulations. In practice, 95% to 99% of the droplets/particles released from cosmetic sprays have aerodynamic equivalent diameters > 10 µm, with propellant sprays yielding a greater fraction of droplets/particles < 10 µm compared with pump sprays.[26,27] Therefore, most droplets/particles incidentally inhaled from cosmetic sprays would be deposited in the nasopharyngeal and thoracic regions of the respiratory tract and would not be respirable (i.e., they would not enter the lungs) to any appreciable amount.[28,29] In addition, Glycine Max (Soybean) Seed Extract and Glycine (Max) Soybean Lipids are reported to be used in face powders, and could possibly be inhaled. The concentrations of these formulations were not reported. 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.[30-32]

The soy-derived ingredients are not restricted from use in any way under the rules governing cosmetic products in the European Union.[33]

Non-Cosmetic

Food

Soy has been a common staple in Asian diets for thousands of years, and is also currently present in modern Western diets. Soybeans can be processed to be used in or as food products such as soy milk, soy sauce, soy curds, tofu, miso, cheese, candies, ice cream, baked goods, and oil.[34] In addition, soy can be found in infant formulas. Soybeans and soybean constituents are commonly used as food fortifiers as their protein content is high. Soybean hulls are commonly used in poultry and swine feeding.[18]

Industrial

Soybean meal and soybean proteins are used in the manufacture of synthetic fiber, adhesives, varnishes, paints, and pesticides.[13,34] In addition, soybeans are used for biodiesel fuel, upholstery, candles, ink, crayons, lubricants, and hydraulic fluid.[35] Soybean hulls are used in the treatment of wastewater.[20]

Medicine

Soybean germ extract has been reported to be used in herbal medication for the treatment of menopausal symptoms.[14] Soy products are also taken as supplements to alleviate high blood pressure/cholesterol, and to increase bone health.[36] None of the ingredients included in this report are used in US FDA-approved medical preparations, however, soybean oil is used in an FDA-approved, intravenous medication, used to provide a source of calories and essential fatty acids for patients requiring parenteral nutrition.[37]

TOXICOKINETIC STUDIES

When rats were given a single oral dose of a soybean extract containing 74 µmol genistein and 77 µmol daidzein/kg as conjugates, the urinary excretion of daidzein and genistein was 17.9% and 11.9%, respectively, over a 48-hour post-dose period.[14] No other details regarding this study were provided. In a human study, 11 German post-menopausal women were given a bolus dose of a commercial soy extract.[38] Sulphoglucuronides were the major metabolites of daidzein and genistein in the plasma, and 7-*O*-glucuronides were the predominant metabolites in the urine.

TOXICOLOGICAL STUDIES

Acute Toxicity Studies

No acute oral, dermal, or inhalation toxicity studies were discovered in the published literature regarding these soy-derived ingredients, and no unpublished data were submitted. However, a study regarding the oral toxicity of a soybean hull extract was found and is summarized below.

Oral

Nine male and nine female Sprague-Dawley rats, as well as 42 male and 44 female C57BL/6 mice were given a single oral dose of black soybean hull extract (2.5 g/kg bw) via gavage.[19] Control animals were given purified water. Rats were observed for 14 days, and mice were observed for 15 days for signs of morbidity or mortality. No deaths, significant decreases in body weight, or gross pathological abnormalities were observed in either species. The LD_{50} was reported to be greater than 2.5 g/kg bw in rats and mice.

Short-Term Toxicity Studies

No short-term dermal or inhalation studies were discovered in the published literature, and no unpublished data were submitted.

Oral

Glycine Soja (Soybean) Extract

The potential toxicity of a hot water extract of black soybeans was studied.[15] Sprague-Dawley IGS rats (6/sex/group) were given 0, 0.5, 1.5, or 5% black soybean extract in the diet for 28 days. No deaths or abnormalities regarding the general conditions of the animals were reported throughout the study. At week 4, a statistically significant increase in urinary potassium values were found in females receiving 5% black soybean extract compared to controls. No treatment-related hematological adverse effects were observed. Platelet count levels were significantly lower in all dosed males, however, changes were minimal and values were within historical control data. Significant elevation of mean

corpuscular volumes and reticulocytes levels were noted in the highest dosed males, however, these changes were also minimal and values were within historical control data. A statistically significant increase in alkaline phosphatase enzymes was found in male rats given 1.5% black soybean extract; however, these changes were not dose-dependent. A statistically significant lowering of relative epididymis weights were found in all extract-dosed males. In addition, a statistically significant but non-dose-dependent elevation of relative heart weight was found in females given 0.5% black soybean extract.

Subchronic Toxicity Studies

No subchronic dermal or inhalation studies were discovered in the published literature, and no unpublished data were submitted.

Oral

Glycine Soja (Soybean) Flour

Soluble soybean fiber (SSF) was given in the diet to Sprague-Dawley CD rats (20/sex/group) at concentrations of 2, 3, and 4%, for three months.[39] A separate group was given an untreated diet, and served as the control. The SSF was extracted from the fibrous residue in the production process of soy protein. The estimated amount of fiber in the SSF was approximately 72-77%. There were no test article related deaths during the study. In both sexes, weight gain in all dose groups during weeks 2-7 was low compared to the controls; however this effect was not dose-related. By the end of the period, weight gain differences were minimal in dosed groups versus control animals. Decreased food consumption was noted in males (weeks 2-5; all dose levels) and in females (weeks 2-4; all dose levels). This was followed by a period of increased food intake in both males (weeks 8-10; all dose levels) and females (weeks 8-11; all dose levels). In all treated males, an increased erythrocyte and decreased reticulocyte count was noted, however, these effects were not dose-dependent. In females, there was a slight, but dose-related increase in the hematocrit and erythrocyte counts of animals of the 3 and 4% dose groups. A reduction in spleen weight was noted in all dosed animals, however this effect was not dose-dependent, and no other histopathological adverse effects were found relating to this matter.

Glycine Soja (Soybean) Extract

The systemic toxicity of aqueous and ethanolic soybean extracts was studied in F344 rats (40 rats/sex).[40] The grinded extract was mixed into the diet for 13 weeks at doses of 0, 1.25, 2.5, and 5%. Neither mortality nor deterioration in general conditions were observed during the course of the study. Results given in this study did not specify which solvent was used when stating extract-induced effects. Statistically significant body weight reductions were noted in males treated with 5% soybean extract, and in all treated females. Statistically significant decreases in red blood cell count, hematocrit levels, and an increase in mean corpuscular volume were detected in 5% males. This effect was not seen in females. Statistically significant, but minimal increases in total protein, albumin, calcium, and aspartate aminotransferase were found in males treated with 2.5% or higher. In females, significant increases of potassium and decreases in chloride were observed in the 5% group. Males in the 5% group displayed a decrease in absolute heart and spleen weights. Dose-dependent decreases in absolute brain weights were observed in male rats dosed with 2.5% and higher. A statistically significant increase in absolute liver weight was observed, in a dose-dependent manner, in all treated animals. Relative kidney weights were also increased in the highest dosed groups of both sexes. Females in the high-dose group displayed a statistically significant decrease in absolute lung weight. Dose-dependent decreases in the absolute weights of the heart and spleen were observed in females at 2.5% and 5%. Soybean-extract related effects were noted in the prostate, vagina, and ovaries. Male rats in the 5% group displayed epithelial atrophy in the ventral prostate, accompanied by cytoplasmic vacuolation and decreases of the luminal secretory fluid. In female rats treated with 2.5% and above, increased incidences of mucification and atrophy of the vaginal epithelium, as well as increased atretic follicles, were observed.

Chronic Toxicity Studies

Glycine Max (Soybean) Seedcoat Extract

Thirty-three male and 35 female C57BL/6 mice were randomly divided into three groups and fed a diet supplemented with 0, 2, or 5% of a black soybean seedcoat extract (acidic water and ethanol used as the extraction agent) for 26 weeks.[19] A significant reduction in body weights was noted in 5% males compared to 2% males and control males. At week 26, the abdominal fat of 5% males was 40% lower than that of controls. This effect was not seen in females. The white blood cell count in 5% males and red blood cell count, hemoglobin, and hematocrit levels in 5% females were significantly increased compared to control animals. Triglyceride and chloride levels in 5% males were significantly decreased. In female animals, triglyceride and blood urea nitrogen levels were decreased in the 5% group. The final body weight of males in the 5% group was significantly lower than that of control males and 2% males. In 5% males, an increase in the relative weights of the kidney, spleen, and brain was apparent. In the same dosing group, a decrease in the relative weight of the spleen was noted. In 5% females, absolute weights of the heart, liver, and kidney were decreased. No significant changes in final body weights were noted in any dosed females. In animals dosed with both 2% and 5% soybean seedcoat extract, in the

duodenum, slight pigment accumulation in histiocytes of the lamina propria was found. Slight accumulation of pigment in Kupffer cells of the liver was apparent in 5% males and females.

Glycine Soja (Soybean) Flour

Sixty male Wistar rats were divided into three groups and given diets containing 19.1, 42.1, or 79.7% raw soy flour.[41] Each of the three groups was subdivided into two groups, one of which was fed ad libitum, and the other a single 4-hour meal per day. Two weeks after the start of the experiment, 5 rats per group were subjected to an injection of azaserine (0.5 mg/100 g bw), dissolved in 0.5 mL sterile saline. Injections were given once a week for 20 weeks. Rats were given their respective diets for up to 12 months. Azaserine injections had no effect on food intake or body weight. A significant decrease in food intake and body weight was noted in animals receiving increased levels of raw soy flour in the diet ($P < 0.01$). Animals fed one meal per day containing 19.1% raw soy flour reached 85% of the body weight of their ad libitum-fed counterparts. Animals fed diets containing 42.1% and 79.7% raw soy flour reached 76 and 62% of the body weight of the ad libitum-fed rats, respectively. Pancreas weights increased as the level of raw soy flour in the diet increased. Approximately 45% of all animals used in the experiment died prior to study termination. In rats fed 19.1% raw soy flour, 25% of rats fed ad libitum were alive at the end of the experiment, while 75% of rats fed only once per day survived until study termination. In rats fed 42.1% raw soy flour, 80% of the meal-fed animals survived vs. 62.5% in the ad libitum group. Carcinogenic effects observed in this study can be found in the Carcinogenicity section of this report.

DEVELOPMENTAL AND REPRODUCTIVE TOXICITY (DART) STUDIES

No DART studies were discovered in the published literature regarding these soy-derived ingredients, and no unpublished data were submitted. However, a study analyzing the reproductive effects of orally ingested soybean was found and included below.

The potential reproductive toxicity of the soybean was tested in 20 male and 60 female rats.[42] The rats were treated with processed soybean meal at 0, 100, 200 and 300 mg/kg bw for 65 days. The test substance was administrated via diet. No statistically significant effect of soybean meal on the weight of the testes and epididymis was observed. Sperm viability and sperm count were significantly reduced in a dose-dependent manner. In addition, sperm head abnormality was significantly increased in a dose-dependent manner. Rats in the control group displayed seminiferous tubules at various stages of development. Rats in the 100 mg/kg bw group had testicular tissues with compacted interstitial spaces, mild hemorrhaging along the Sertoli's cells, and slight degeneration of the spermatids. Rats treated with 200 mg/kg bw displayed similar effects, and rats treated with 300 mg/kg bw displayed adverse effects such as testicular tissues with inflammation of interstitial cells, severe hemorrhaging along the Sertoli's cells, and excessive degeneration of spermatids, and necrosis. The conception rate of female rats sired by males in the control and treated groups were reduced in a dose-dependent manner. No other effects regarding treated female rats were observed.

GENOTOXICITY

No genotoxicity studies were discovered in the published literature, and no unpublished data were submitted.

CARCINOGENICITY STUDIES

No carcinogenicity studies were discovered in the published literature, and no unpublished data were submitted.

ANTI-CARCINOGENICITY STUDIES

Glycine Soja (Soybean) Flour

Male albino mice (n = 216) were separated into 3 groups and fed diets of either raw soy flour, heated soy flour, or casein for up to 18 months.[43] The soy flour diet consisted of soy flour (42.1%), glucose (15%), non-nutritive fiber (5%), corn oil (5.5%), lard (2.5%), DL-methionine (0.1%), choline chloride (0.2%), vitamin mix (2%), mineral mix (5%), and dextrin (22.6%). Animals were also given an injection of either azaserine (10 mg/kg/bw) or 0.9% sodium chloride. Growth of mice was significant lower ($P < 0.01$) in mice given raw soy flour compared to mice given heated soy flour or casein. The injections with azeserine and sodium chloride did not seem to have an effect. No statistically significant carcinogenic/tumorigenic effects were noted.

In a different 15-month study, 54 Syrian Golden male hamsters were divided into four groups and given raw soy flour, heated soy flour, raw soy flour injected with *N*-nitrosobis(2-oxopropyl)amine (BOP), or heated soy flour injected with BOP.[43] BOP injections were given at a level of 10 mg/kg bw on days 7 and 14. Animals not given a BOP injection received an injection of 0.9% sodium chloride. The soy flour composition is the same as was used in the experiment above. Animals fed raw soy flour displayed a slower growth rate ($P < 0.01$) than those fed heated soy flour. At 7 - 8 months, animals injected

with BOP lost weight at a significantly ($P < 0.05$) faster rate than animals injected with saline. No significant difference was found in the weights of the pancreas in any of the groups by the end of the study. In groups that did not receive BOP, tumor incidence was quite low; however, in groups that did receive BOP, tumor incidence was increased. Seven out of 8 surviving animals that were given heated soy flour and BOP injections had pancreatic adenomas, and 5 had pancreatic adenocarcinomas. One out of 11 surviving BOP-injected animals given raw soy flour had a pancreatic adenoma, and no adenocarcinomas.

Sixty male Wistar rats were divided into three groups and given diets containing 19.1, 42.1, or 79.7% raw soy flour.[41] Each of the three groups was subdivided into two groups, one of which was fed ad libitum, and the other one 4-hour meal per day. Two weeks after the start of the experiment, 5 rats per group were subjected to an injection of azaserine (0.5 mg/100 g bw), dissolved in 0.5 mL sterile saline. Injections were given once a week for 20 weeks. Rats were given their respective diets for up to 12 months. Twenty-seven rats died prior to the end of the study. Among these animals, pancreatic nodules were observed in 1/11, 3/7, and 6/9 rats given 19.1, 42.1, 79.7% raw soy flour, respectively. In rats that were sacrificed after 10-12 months on the experiment, in the absence of azaserine injections, the incidence of nodules was low and unaffected by the feeding regime. Animals that received azaserine injections had a much higher incidence of nodules, which increased with the level of raw soy flour in the diet. No nodules were found in any other organ examined. Other toxic effects observed during this study can be seen in the Chronic Toxicity Studies section of this report.

OTHER RELEVANT STUDIES

Effect on Cancer Cell Proliferation

Glycine Soja (Soybean) Extract

The potential anticarcinogenic ability of an ethanolic extract of the black soybean on A549 lung cancer cells was studied.[9] The black soy ethanol extract was dissolved in 10% dimethyl sulfoxide (DMSO) at a concentration of 10 mg/mL. The extract was used to prepare final diluted concentrations of 6.25, 12.5, 50, 100, 200, 400, and 800 µg/mL. Cancer cells were cultured for 1 week before exposure to the test substance. The cells were then subjected to 100 µL of each dilution of the test substance as stated above. Each experiment was performed three times, and results were averaged. After incubation for 48 hours, cell viability was measured using a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. The extract exhibited cytotoxic activity in a concentration-dependent manner in A549 cells. Percent inhibition of A549 lung cancer cells by the soy ethanol extract was 5.2, 4.4, 20.6, 37, 52.8, 60.8, 68.7, and 83.8% when tested at concentrations of 6.25, 12.5, 50, 100, 200, 400, and 800 µg/mL, respectively.

The effect of black soybean extract on the suppression of the proliferation of human gastric cancer (AGS) cells was studied.[17] For this study, the soybean extract was obtained by extracting black soybean with acidified aqueous acetone. AGS cells were plated at a density of $5x10^3$ cells/well in 96-well plates. The effect of the extract on the growth of AGS cells was investigated using an MTT assay. After incubation (24 hours), the extract was added to the plates in concentrations of 1-5 mg/mL, and incubated for another 48 hours. The extract inhibited growth of AGS cells in a dose-dependent manner. When a concentration of 3 mg/mL extract was used on the AGS cells, cell viability was significantly decreased compared to control cells ($p < 0.05$). Approximately 65.7, 38.8, and 22.5% cells survived after treatment with 3, 4, and 5 mg/mL of black soybean extract. The same procedure was performed on normal rat fibroblast cells. No cytotoxicity was observed when black soybean extract was used on these cells.

Glycine Max (Soybean) Leaf Extract

The anti-cancer properties of an ethanolic extract of soybean leaves (SLE) was studied in both human colon cancer cells (HCT116) and human lung cancer cells (H1299).[6] The treatment of the HCT116 cells with SLE at concentrations of 125, 250, and 500 µg/mL for 72 hours resulted in a significant inhibition of growth (by 34-89%). When HCT116 cells were treated with the same concentrations of SLE for 96 hours, growth inhibition increased (by 62-87%). Treatment of H129 cells with SLE (125, 250, and 500 µg/mL) inhibited growth by 45-85%. In both types of cancer cells, the growth inhibitory effects of SLE increased with increasing concentrations of SLE, showing a significant dose-response relationship. In addition to inhibition of growth, the effect of SLE on adhesion and migration of the human cancer cells was also studied. When H1299 cells were treated with SLE at 500 µg /mL, a significant inhibition of migration was noted. Treatment of HCT116 and H1299 cells with SLE also inhibited cell adhesion to fibronectin by 21-31% (at 125-500 µg/mL) and 14% (at 500 µg/mL), respectively.

Epidermal Hyperplasia Inhibition

The possible inhibition of retinoid-induced epidermal hyperplasia was studied in 7 human skin organ cultures.[44] Cultures of human skin were incubated with 1 µg/mL of 14-all *trans* retinoic acid (14-all *trans* RA) for 8 days. A soy extract was prepared by mixing 250 mg of soy powder in 2 mL of a basal medium. A DMSO extract was also prepared by dissolving 250 mg of soy powder in 1 mL of solvent. All of the soy dissolved in the DMSO, and this solution was used as a control. Hyperplasia-induced organ cultures were treated with soy extracts at 4, 20, or 40 µg/mL. In the presence of 40

µg/mL soy extract, retinoid-induced hyperplasia was reduced by 41% relative to the retinoid response in the absence of soy. Sixteen percent inhibition was observed at 4 µg/mL, and 32% inhibition was observed at 20 µg/mL.

Effects on Pigmentation

An aqueous extract of black soybean sprouts was examined for whitening capacity.[10] Whitening capacity was measured via the measurement of tyrosinase-inhibition. Tyrosinase inhibition capacity of the extract, when used at 40 mg/mL, reached 98%. Inhibition capacity reached 60-95% after treatment with 4 mg/mL of the extract, and 40% after treatment with 2 mg/mL of the extract.

Estrogenic Activity

Methanol extracts were prepared from soybeans and evaluated for estrogenic activity.[45] The estrogenic activity was analyzed by measuring the MCF-7 (breast cancer cell line) cell proliferation in response to various concentrations of the extract (0.1 – 100 µg/mL). Soybean extract (0.1 µg/mL) caused an increase of estrogenic activity to approximately 35 %, while at 100 µg/mL, estrogenic activity was increased to 90%. In order to determine whether the induced cell proliferation was mediated via an estrogen receptor (ER)-dependent mechanism, the soybean extract (100 µg/mL) was tested in combination with the pure estrogen antagonist, 7α-[9-[(4,4,5,5,5-pentafluoropentyl)-sulfinyl]nonyl] estra-1,3,5(10)-triene-3,17β-diol (ICI 182,780). Testing of the soybean extract in combination with ICI 182,780 resulted in decreased estrogenic activity (below 0%). A reported gene assay was also performed using human embryonic kidney cells (HEK 293 cells) in order to determine whether the estrogenic effects of the extracts were mediated via ERα and/or ERβ. Preferential agonist activity toward ERβ was observed. For ERβ transcriptional activation, the maximal value obtained at 100 µg/mL was 79.7%, compared to 53.2% for ERα transcriptional activation.

A study was performed to analyze the estrogenic effects of soybean extract, obtained using different extraction methods, on the skin of 64 Sprague-Dawley female rats (8/group).[11] The specific soy extracts were administered via gavage each day for one month. Animals in group A were untreated, animals in group B received carboxymethyl cellulose (0.5%); this solution was also used to dilute the extracts for administration to the experimental animals. Group C received an n-hexane soy extract at a dose of 100 mg/kg and group D received the same extract at a dose of 200 mg/kg. Groups E and F received ethyl-acetate soy extracts at doses of 100 and 200 mg/kg, respectively, and groups G and H received an ethanolic soy extract at 100 and 200 mg/kg, respectively. (Details about the preparation of these extracts can be seen in the Method of Manufacturing section of this report.) A statistically significant reduction in the number of estrogen receptor-positive cells (per 10 high-power fields) and an increase in the collagen layer thickness were observed ($p < 0.05\%$) in all groups treated with a soy extract. The thickness of the collagen layer of the rats in group F (1154.93 µM) was significantly higher than that of the rats in group A (864.32 µM). The number of estrogen receptor-positive cells in group D (2.37) was significantly reduced compared to that of group A (6.87), B (8.25), and C (4.75). The number of estrogen receptors in all soy extracted – treated groups were decreased compared to that of the controls.

Antimicrobial Activity

The antimicrobial activities of an ethanolic leaf and seed extract of soybean were studied.[22] The following microorganisms were subjected to different concentrations (50, 75, 100, and 150 mg/mL) of the dried extracts: *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus niger*. All concentrations of the soybean extract resulted in inhibition of the tested pathogens, excluding the 50 mg/mL concentration, where the extracts showed inhibition only on fungal strains. At 75, 100, and 150 mg/mL, inhibitory activity of the ethanolic soybean seed extract on *E. coli* was measured to be 2.62, 4.66, and 6.89, respectively. The inhibitory activity of the ethanolic soybean leaf extract on *E. coli* for the same test concentrations were 3.64, 6.32, and 9.60, respectively. Inhibitory activity increased in a concentration-dependent manner for all tested microorganisms.

Cytotoxicity

A trade name mixture containing water (100% q.b. to 100% w/w), Glycine Max Callus Culture (13 – 18%), citric acid (1.5%), sodium benzoate (0.2%), and potassium sorbate (0.1%), was tested for cytotoxicity.[46] The product showed a half maximal inhibitory concentration (IC_{50}) greater than 5 µL/mL on human keratinocytes with an MTT assay. No other details regarding this study were provided.

Immunotoxicity

BALB/c mice were dorsally shaved and epicutaneously exposed to a crude soybean extract (50 mg/mL) containing 0.5% sodium dodecyl sulfate in distilled water ($n = 9$) or distilled water alone ($n = 8$).[47] Each week, the skin of the animals was shaved and stripped 10 times using adhesive tape. Mice were also intraperitoneally injected with a mixture of midazolam, butorphanol, and medetomidine. Three times a week for 5 weeks, 50 µL samples were applied epidermally. Various specific immunoglobulin E (IgEs) secreted in response to 7S globulin (Gly m 5), 11S globulin (Gly m 6), Gly m 3, and Gly m 4 were measured using enzyme-linked immunosorbent assays or immunoblots. Percutaneous exposure to the soybean extract caused a systemic secretion of soybean-specific IgEs. Of the soy proteins, both 7S and 11S globulins were allergenic in 67% of tested mice. Of the 3 subunits of 7S globulin, it was determined that the β subunit is especially prone to eliciting secretion of soybean-specific IgEs following percutaneous exposure.

DERMAL IRRITATION AND SENSITIZATION

Irritation

Glycine Soja (Soybean) Extract

Patch tests were performed over an area of 5 cm x 4 cm on the forearms of 11 subjects.[48] The test material was a cosmetic water-in-oil emulsion incorporating 4% soybean extract. The amount of test substance applied was not noted. Following application of the test substance, a surgical dressing was used to cover the marked area. It was not stated whether or not the dressing used was occlusive. After 48 hours, the dressing was removed and forearms were washed with physiological saline. Irritation was not observed in any of the subjects.

Glycine Max (Soybean) Sprout Extract

The irritation potential of a black soybean sprout extract (4 or 40 mg/mL) was studied in 30 subjects (15/sex).[10] Extracts were applied on the arm, under a patch, for 24 hours. It was not stated whether or not the dressing used was occlusive. No other details regarding this study were provided. No signs of irritation were observed in any subject.

Sensitization

No sensitization data were found in the published literature, and unpublished data were not submitted.

OCULAR IRRITATION STUDIES

In Vitro

Glycine Max (Soybean) Sprout Extract

The potential irritation of black soybean sprout extract (40 mg/mL and 4 mg/mL) was studied using a chicken chorioallantoic membrane (CAM) assay.[10] Sodium dodecyl sulfate (0.4% and 4%) was used as a positive control, and 0.9% saline was used as a negative control. Similar results were observed in both the negative control group and groups treated with the soybean sprout extract. The test substance was considered to be non-irritating. No other details regarding this study were provided.

CLINICAL STUDIES

Case Reports

A 55-year-old woman with a 5-month history of reacting to a facial cosmetic cream developed erythema and swelling of the face after using a night cream containing soybean extract.[49] Patch tests were performed using different dilutions of soybean extract, the night cream itself, components of the night cream, and standard cosmetic/facial ingredients. The following allergens were tested: para-phenylenediamine (1% in petrolatum (pet.)), fragrance mix (8% pet.), cocamidopropyl betaine (1% pet.), night cream, ceramide 3 and soybean extract (2% pet.), ceramide 3 (5%), ceramide 3 (2%), and three different dilutions of soybean extract (1, 10, and 20%). When the soybean extract dilutions were applied under occlusive patches to the forearm and read at 30 minutes, slight erythema was observed at the 20% dilution. Palpable erythema was observed after 36 hours at the 10 and 20% dilution. Patch tests using both concentrations of ceramide 3 were negative, however, the patch test using ceramide 3 and soybean extract (2%), yielded positive results. Positive results were obtained for all dilutions of the soybean extract on days 2 and 7. Para-phenylenediamine and cocamidopropyl betaine resulted in positive results on day 4, and the fragrance mix yielded positive results on day 2 and 4. The patient reported previous consumption of soybeans without adverse reactions and was subjected to an allergen-specific IgE test to soybean, which was negative.

A 30-year-old female esthetician with atopic dermatitis and severe hand eczema developed anaphylactic symptoms (systemic urticaria, dyspnea, and hypotension) after consuming soy products.[50] Prior to working as an esthetician, she did not experience hand eczema or soy food allergies. Beginning at the age of 23, she began to touch cosmetic lotions frequently at the work place. Several months later, she noticed eczema on her fingers. At 28 years old, she experiences severe symptoms such as systemic urticaria and dyspnea after consumption of soy products. Examinations revealed the following: a total serum immunoglobulin (IgE) level of 3280 international units (IU)/mL, thymus and activation-regulated chemokine level of 715 pg/mL, and lactase dehydrogenase levels of 274 units (U)/L. Specific IgE antibodies were detected for soy (19.3 U_A/mL), Japanese cedar (4.72 U_A/mL) and Japanese white birth (1.24 U_A/mL). Skin pricks test were preformed using soy extract (10 mg/mL), the cosmetic lotion containing soy extract used by the patient, and a commercially available soy milk. All tests yielded positive results. Skin prick tests performed on three healthy volunteers using the same cosmetic lotion yielded negative results.

Occupational Exposure

The allergenicity to soybean hull in subjects exposed to different levels of soybean dust inhalation (SDI) in Argentina was studied.[51] Exposure to SDI was defined as follows: (1) direct = occupational, (2) indirect = proximity to soybean fields or grain elevators, and (3) urban = urbanized areas without a known source of SDI. Two different types of groups were studied. Group 1 consisted of 365 patients who were clinically diagnosed with asthma or allergic rhinitis. Group 2 consisted of 50 healthy subjects. All participants were given a standard questionnaire, and were subjected to a prick skin test (ST) with common allergens and a soybean hull extract. In addition, specific IgE and immunoglobin G4p (IgG4) secreted in response to soybean hulls were measured in the sera of 51 patients from group 1 with a positive ST to soybean hull, and in all subjects from group 2. From group 1, 15.3% of subjects had a positive ST to soybean hulls. No subjects from group 2 had a positive ST. In group 1, positives STs to soybean hull were reported for 38.7, 20.3, and 8.2% of the patients with direct, indirect, and urban exposures, respectively. The percentage of positive soybean hull-specific IgE secretion in groups 1 and 2 were 39.2% and 10%, respectively, and for IgG4 were 27.4% and 12%, in groups 1 and 2, respectively. IgG4 levels in group 1 were significantly higher in subjects with direct exposure compared to subjects with indirect or urban exposure.

In a different study, workers from three soybean-processing plants in South Africa were studied with a respiratory questionnaire and estimation of atopy.[52] A total of 144 employees completed the questionnaire, and 136 gave blood samples for analysis of specific IgE levels. The processes in all three worksites were based on similar milling techniques. Soybeans arrive at the processing mill, are off-loaded, and stored. The beans are then de-hulled, subjected to cooking, milled, and bagged. According to the questionnaire, 38 individuals reported either an upper or lower work-related respiratory symptom. Among these individuals, eight employees reported upper respiratory symptoms in the absence of any lower respiratory symptoms. Twenty-two employees reported lower-respiratory symptoms only (cough, wheezing, or chest tightness). The remaining eight employees reported both upper and lower respiratory symptoms. Cough and chest tightness were the most commonly reported symptoms, followed by nasal irritation and wheezing. Altogether, 33.1% (45/136) of workers were atopic, and 14% (19/136) of workers exhibited sensitization to soybean allergens.

SUMMARY

The safety of 28 soy-derived ingredients as used in cosmetics is reviewed in this CIR safety assessment. All ingredients reviewed in this report are derived from the soybean plant (*Glycine max* or *Glycine soja*). According to the *Dictionary*, most of these ingredients are reported to function as antioxidants, skin protectants, skin-conditioning agents – miscellaneous, and hair-conditioning agents; however, other functions are also reported. These ingredients are commonly used in food and food products. Because daily exposures via ingestion would cause a much greater systemic exposure than from cosmetic exposure, toxicity from dermal applications was the focus of this report.

Soybeans contain many bioactive phytochemicals, such as phenolic acids, flavonoids, isoflavanoids, saponins, phytosterols, and sphingolipids. These phytochemicals vary based on geographic location, specific parts and color of the bean/plant.

According to 2019 VCRP survey data, Glycine Soja (Soybean) Seed Extract is reported to be used in 395 formulations, 273 of which are leave-on formulations, and Glycine Soja (Soybean) Flour is reported to be used in 66 formulations The results of the concentration of use survey conducted by the Council indicate Glycine Soja (Soybean) Lipids has the highest concentration of use in a leave-on formulation; it is used at up to 0.65% in lipsticks. Additionally, inhalation of Glycine Soja (Soybean) Seed Extract is possible, as it was reported to be used at 0.000001% in hair sprays.

When rats were given a single oral dose of a soybean extract containing 74 µmol genistein and 77 µmol daidzein/kg as conjugates, the urinary excretion of daidzein and genistein was 17.9% and 11.9%, respectively, over a 48-hour post-dose period. When humans were given a bolus dose of a commercial soy extract, sulphoglucuronides were the major metabolites of daidzein and genistein the in the plasma, and 7-O-glucuronidse were the predominant metabolites in the urine.

When 18 Sprague-Dawley rats and 86 C57BL/6 mice were given a single oral dose of black soybean hull extract (2.5 g/kg/bw) via gavage, the LD_{50} was reported to be greater than 2.5 g/kg bw in both species. In a different study, Sprague-Dawley IGS rats (6/sex/group) were given up to 5% black soybean extract in the diet for 28 days. No deaths were reported throughout the study, however a statistically significant increase in phosphatase enzymes was found in male rats given 1.5% black soybean extract. In addition, a statistically significant but non-dose-dependent elevation of relative heart weight was found in females given 0.5% black soybean extract. In a different study, SSF was given to Sprague-Dawley CD rats (20/sex/group) at concentrations up to 4% for three months. A slight, but dose-related increase in the hematocrit and erythrocyte count at the 3 and 4% level was noted. In a 13-week toxicity study, the systemic toxicity of aqueous and ethanolic soybean extracts (up to 5%) was studied in F344 rats (40 rats/sex). Statistically significant body weight reductions were noted in males treated with 5% soybean extract, and in all treated females. Statistically significant, but minimal increases in total protein, albumin, calcium, and aspartate aminotransferase were found in males treated with 2.5% or higher. Dose-dependent, statistically significant changes in organ weights compared to control animals were also noted. In a different study, 33 male and 35 female C57BL/6 mice were given up to 5% black soybean seedcoat extract in the diet for 26

weeks. Significant body weight reduction was noted in high-dosed males. Significant reductions in triglyceride, hemoglobin, and hematocrit levels were noted in high-dosed females. Relative weights of the kidney, spleen, and brain were increased in high-dosed males. In animals dosed with both 2% and 5% soybean seedcoat extract, in the duodenum, slight pigment accumulation in histiocytes of the lamina propria was found. Slight accumulation of pigment in Kupffer cells of the liver was apparent in 5% males and females.

A chronic toxicity study was performed on 60 male Wistar rats given up to 79.7% raw soy flour ad libitum or as a single meal per day. Azaserine injections were also given to select animals. Approximately 45% of all animals died prior to the termination of the experiment. Pancreas weights increased as the level of raw soy flour in the diet increased.

The reproductive toxicity of the soybean was tested in 20 male and 60 female rats. Rats were given processed soybean meal at up to 300 mg/kg bw for 65 days. Rats in the 100 mg/kg/bw group had testicular tissues with compacted interstitial spaces, mild hemorrhaging along the Sertoli's cells, and slight degeneration of the spermatids. Rats treated with 200 mg/kg/bw displayed similar effects, and rats treated with 300 mg/kg /bw displayed adverse effects such as testicular tissues with inflammation of interstitial cells, severe hemorrhaging along the Sertoli's cells, and excessive degeneration of spermatids, and necrosis. The conception rate of female rats sired by males in the control and treated groups were reduced in a dose-dependent manner. No other effects regarding treated female rats were observed.

Male albino mice (n = 216) were given a diet containing raw soy flour, heated soy flour, or casein for up to 18 months in an anti-carcinogenicity study. Animals were also given an injection of either azaserine (10 mg/kg bw) or 0.9% sodium chloride. Growth of mice was significant lower ($P < 0.01$) in mice given raw soy flour compared to mice given heated soy flour or casein. The injections with azeserine and sodium chloride did not seem to have an effect. In a 15-month study, 54 Syrian Golden male hamsters were divided into four groups and given raw soy flour, heated soy flour, raw soy flour injected with BOP, or heated soy flour injected with BOP. No significant difference was found in the weights of the pancreas in any of the groups by the end of the study. In groups that did not receive BOP, tumor incidence was quite low; however, in groups that did receive BOP, tumor incidence was increased. Seven out of 8 surviving animals that were given heated soy flour and BOP injections had pancreatic adenomas, and 5 had pancreatic adenocarcinomas. One out of 11 surviving BOP-injected animals given raw soy flour had a pancreatic adenoma, and no adenocarcinomas. In a different carcinogenicity study, 60 male Wistar rats were given up to 79.7% raw soy flour in the diet, either ad libitum or as a single meal per day. Injections of azaserine were also given to select rats. Among the 27 animals that did not survive the study, pancreatic nodules were observed in 1/11, 3/7, and 6/9 rats given 19.1, 42.1, 79.7% raw soy flour, respectively. In rats that survived the study, in the absence of azaserine injections, the incidence of nodules were low and unaffected by the feeding regime. Animals that received azaserine injections had a much higher incidence of nodules, which increased with the level of raw soy flour in the diet.

Studies were performed in order to analyze the effects of soy-derived extracts on cancer cell proliferation. An ethanolic soybean extract inhibited cytotoxic activity in A549 cells in a concentration-dependent manner. The potential of a soybean extract to inhibit the proliferation of cancer cells was also studied on AGS cells. Approximately 65.7, 38.8, and 22.5% cells survived after treatment with 3, 4, and 5 mg/mL of black soybean extract. The same procedure was performed on normal rat fibroblast cells. No cytotoxicity was observed when black soybean extract was used on these cells. In a different assay, HCT116 and H1299 cells were exposed to an ethanolic extract of soybean leaves. In both types of cancer cells, the growth inhibitory effects of SLE increased with increasing concentrations of SLE, showing a significant dose-response relationship. In addition to inhibition of growth, the effect of SLE on adhesion and migration of the human cancer cells was also studied.

The possible inhibition of retinoid-induced epidermal hyperplasia was studied in 7 human skin organ cultures. In the presence of a 40 µg/mL soy extract, retinoid-induced hyperplasia was reduced by 41% relative to the retinoid response in the absence of soy.

An aqueous extract of black soybean sprouts was examined for whitening capacity via the measurement of tyrosinase-inhibition. Tyrosinase inhibition capacity of the extract, when used at 40 mg/mL, reached 98%.

Methanol extracts were prepared from soybeans and evaluated for estrogenic activity. Soybean extract (0.1 µg/mL) caused an increase of estrogenic activity to approximately 35 %, while at 100 µg/mL, estrogenic activity was increased to 90%. Testing of the soybean extract in combination with ICI 182,780 resulted in decreased estrogenic activity (below 0%). A reported gene assay was also performed using human embryonic kidney cells (HEK 293 cells) in order to determine whether the estrogenic effects of the extracts were mediated via ERα and/or ERβ. Preferential agonist activity toward ERβ was observed. For ERβ transcriptional activation, the maximal value obtained at 100 µg/mL was 79.7%, compared to 53.2% for ERα transcriptional activation. A study was performed to analyze the estrogenic effects of orally administrated soybean extract obtained using different extraction methods on the skin of 64 Sprague-Dawley female rats (8/group). The number of estrogen receptors in all soy extracted –treated groups were decreased compared to that of the controls.

The potential antimicrobial effect of an ethanolic soybean leaf and seed extract was studied. Microbial-inhibition was observed in a concentration-dependent manner for all tested organisms (*Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus niger).*

A percutaneous immunotoxicity study was performed on BALB/c mice. Mice were dermally exposed (after tape stripping 10x) to crude soybean extract (50 mg/mL, 3 times a week). Exposure to the soybean extract resulted in an increase of circulatory soybean-specific IgEs. Of the soy proteins, both 7S and 11S globulins were allergens in 67% of tested mice.

A 48-hour patch test was performed on 11 subjects using a cosmetic formulation containing 4% soybean extract. No irritation was observed. A 24-hour patch test performed on 30 subjects using 4 or 40 mg/mL black soybean sprout extract yielded negative results.

A CAM assay was performed using a soybean sprout extract revealed no potential irritation. A trade name mixture containing 87.5% Glycine Soja (Soybean) Seed Extract was considered to be non-irritating to the eyes.

According to a case study, a 55-year-old woman with a 5-month history of reacting to a facial cosmetic cream developed erythema and swelling of the face after using a night cream containing soybean extract. Patch tests were performed using different dilutions of soybean extract, the night cream itself, components of the night cream, and standard cosmetic/facial ingredients. Positive results were obtained for all dilutions of the soybean extract on days 2 and 7. In a different case study, a 30-year-old female esthetician with atopic dermatitis and severe hand eczema developed anaphylactic symptoms after consuming soy products. Skin pricks test were preformed using soy extract (10 mg/mL), the cosmetic lotion containing soy extract used by the patient, and commercially available soy milk. All tests yielded positive results.

Allergenicity to soybean hull was studied in an occupational exposure study. Positive skin prick tests to soybean hull were reported for 38.7, 20.3, and 8.2% in subjects with direct (occupational), indirect (proximity to soybean fields or grain elevators), or urban (no known source of soy dust inhalation) exposures, respectively. Another occupational study was performed, assessing soybean-processing plant workers in South Africa. In 38/144 individuals that reported either an upper or lower work-related respiratory symptom, eight employees reported upper respiratory symptoms in the absence of any lower respiratory symptoms, 22 reported lower-respiratory symptoms only (cough, wheezing, or chest tightness), and the remaining eight employees reported both upper and lower respiratory symptoms.

INFORMATION SOUGHT

The following data are requested for the soy-derived cosmetic ingredients reviewed in this safety assessment.

1.) Dermal toxicity data
2.) Human skin irritation and sensitization data at maximum concentrations of use
3.) Method of manufacturing data as used in cosmetics
4.) Ingredient compositions as used in cosmetics
5.) Confirmation that the following Glycine Max (Soybean) and Glycine Soja (Soybean) ingredients are equivalent, since the accepted scientific name for *Glycine soja* is *Glycine max*: Fiber, Phytoplacenta Extract, Seedcake Extract, Seed Extract and Sprout Extract
6.) Any additional data that would inform this safety assessment

TABLES

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

Ingredient	Definition	Function
Glycine Max (Soybean) Callus Culture	Glycine Max (Soybean) Callus Culture is a suspension of the cultured callus cells of *Glycine max*.	Antioxidants; Humectants; Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Callus Culture Extract	Glycine Max (Soybean) Callus Culture Extract is the extract of a culture of the callus of *Glycine max*.	Antifungal Agents; Antioxidants; Hair Conditioning Agents; Skin-Conditioning Agents - Humectant
Glycine Max (Soybean) Callus Extract	Glycine Max (Soybean) Callus Extract is the extract of the callus of *Glycine max* grown in culture.	Antimicrobial Agents; Antioxidants; Hair Conditioning Agents; Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Fiber	Glycine Max (Soybean) Fiber is the fiber obtained from the pulp of the soybean, *Glycine max*.	Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Flower/Leaf/Stem Juice	Glycine Max (Soybean) Flower/Leaf/Stem Juice is the juice expressed from the flowers, leaves and stems of *Glycine max*.	Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Leaf Cell Extract	Glycine Max (Soybean) Leaf Cell Extract is the extract of a culture of the leaf cells of *Glycine max*.	Antioxidants; Skin Protectants
Glycine Max (Soybean) Leaf Extract	Glycine Max (Soybean) Leaf Extract is the extract of the leaves of *Glycine max*.	Antioxidants; Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Phytoplacenta Conditioned Media	Glycine Max (Soybean) Phytoplacenta Conditioned Media is the growth media removed from cultures of the phytoplacenta of *Glycine max* after several days of growth.	Antimicrobial Agents; Hair Conditioning Agents; Skin Protectants; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Phytoplacenta Extract	Glycine Max (Soybean) Phytoplacenta Extract is the extract of the phytoplacenta cells directly isolated from the plant *Glycine max* or grown in culture.	Antimicrobial Agents; Antioxidants; Hair Conditioning Agents; Skin Protectants; Skin-Conditioning Agents - Humectant
Glycine Max (Soybean) Pulp	Glycine Max (Soybean) Pulp is the pulp of *Glycine max*.	Skin-Conditioning Agents - Humectant
Glycine Max (Soybean) Seedcake Extract	Glycine Max (Soybean) Seedcake Extract is the extract of the seedcake of *Glycine max*.	Skin-Conditioning Agents - Emollient
Glycine Max (Soybean) Seedcoat Extract	Glycine Max (Soybean) Seedcoat Extract is the extract of the seedcoat of *Glycine max*.	Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Seed Powder	Glycine Max (Soybean) Seed Powder is the powder obtained from the dried, ground seeds of *Glycine max*.	Exfoliants; Skin-Conditioning Agents - Miscellaneous
Glycine Max (Soybean) Sprout Extract	Glycine Max (Soybean) Sprout Extract is the extract of the sprout of the soybean, *Glycine max*.	Body and Hand Preparations (Excluding Shaving Preparations); Face and Neck Preparations (Excluding Shaving Preparations); Moisturizing Preparations; Shampoos (Non-coloring); Skin Care Preparations, Misc.
Glycine Soja (Soybean) Extract	Glycine Soja (Soybean) Extract is the extract of the whole plant, *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max*.	Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Fiber	Glycine Soja (Soybean) Fiber is the fiber obtained from the pulp of the soybean, *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max*.	Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Flour 68513-95-1	Glycine Soja (Soybean) Flour is the powder prepared from the fine grinding of the soybean, *Glycine max*. The accepted scientific name for *Glycine soja* is *Glycine max*.	Abrasives; Bulking Agents; Viscosity Increasing Agents - Aqueous
Glycine Soja (Soybean) Germ Extract	Glycine Soja (Soybean) Germ Extract is the extract of the germ of *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max*.	Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Hull	Glycine Soja (Soybean) Hull is the outer covering of the soybean, *Glycine soja* The accepted scientific name for *Glycine soja* is *Glycine max*.	Exfoliants; Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Lipids	Glycine Soja (Soybean) Lipids is the alcohol soluble fraction of the gummy portion obtained during the refining of Glycine Soja (Soybean) Oil. It is a blend consisting predominantly of phospholipids, sterols and triglycerides. The accepted scientific name for *Glycine soja* is *Glycine max*.	Hair Conditioning Agents; Skin-Conditioning Agents - Occlusive

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

Ingredient	Definition	Function
Glycine Soja (Soybean) Phytoplacenta Extract	Glycine Soja (Soybean) Phytoplacenta Extract is the extract of the phytoplacenta cells directly isolated from the plant *Glycine soja* or grown in culture. The accepted scientific name for *Glycine soja* is *Glycine max.*	Hair Conditioning Agents; Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Seed	Glycine Soja (Soybean) Seed is the bean of *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max.*	Not Reported
Glycine Soja (Soybean) Seedcake Extract	Glycine Soja (Soybean) Seedcake Extract is the extract of the seedcake of *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max.*	Skin Protectants
Glycine Soja (Soybean) Seed Extract	Glycine Soja (Soybean) Seed Extract is the extract of the seeds of *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max.*	Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Seed Powder	Glycine Soja (Soybean) Seed Powder is the powder obtained from the dried, ground seeds of *Glycine soja*. The accepted scientific name for *Glycine soja* is *Glycine max.*	Abrasives; Bulking Agents; Skin-Conditioning Agents - Miscellaneous
Glycine Soja (Soybean) Seed Water	Glycine Soja (Soybean) Seed Water is an aqueous solution of the steam distillate obtained from the seeds of *Glycine soja.* The accepted scientific name for *Glycine soja* is *Glycine max.*	Skin-Conditioning Agents - Humectant
Glycine Soja (Soybean) Sprout Extract	Glycine Soja (Soybean) Sprout Extract is the extract of the young shoots of the soybean, *Glycine soja.* The accepted scientific name for *Glycine soja* is *Glycine max.*	Skin-Conditioning Agents - Miscellaneous

Table 2. Average constituents in 24 soybean seed extracts (g/100 g)[13]

Carbohydrates	30.16	Alanine	1.915
Sugars	7.33	Aspartic acid	5.112
Fat	19.94	Glutamic acid	7.874
Protein	36.49	Glycine	1.880
Tryptophan	0.591	Proline	2.379
Threonine	1.766	Serine	2.375
Isoleucine	1.971	Water	8.54
Leucine	3.309	Calcium	0.277
Lysine	2.706	Iron	.0175
Methionine	0.547	Magnesium	.280
Phenylalanine	2.122	Phosphorus	.704
Tyrosine	1.539	Potassium	1.797
Valine	2.029	Sodium	.002
Arginine	3.153	Zinc	.00489
Histidine	1.097		

Table 3. Mean nutrient and amino acid values for 38 samples of soybean hulls (%)[18]

Moisture	8.18
Crude fiber	33.32
Nitrogen-free extract	39.18
Ash	4.87
Calcium	0.52
Phosphorous	0.15
Lysine	0.86
Methionine	0.16
Threonine	0.48
Tryptophan	0.15
Arginine	0.65
Histidine	0.31
Leucine	0.82
Isoleucine	0.48
Phenylalanine	0.54
Valine	0.55

Table 4. Frequency (2019) and concentration (2016) of use of soy-derived ingredients.[24,25]

	# of Uses	Conc of Use (%)	# of Uses	Conc of Use (%)	# of Uses	Conc of Use (%)
	Glycine Max (Soybean) Seed Extract		**Glycine Max (Soybean) Phytoplacenta Extract**		**Glycine Soja (Soybean) Extract**	
Totals*	**395**	**0.0066 - 1**	**16**	**NR**	**11[d]**	**NR**
Duration of Use						
Leave-On	*273*	*0.0066 – 1*	*13*	*NR*	*9[d]*	*NR*
Rinse-Off	*121*	*0.0066*	*3*	*NR*	*2[d]*	*NR*
Diluted for (Bath) Use	*1*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	35	0.0066	1	NR	NR	NR
Incidental Ingestion	22	NR	NR	NR	NR	NR
Incidental Inhalation-Spray	6; 93[a]; 70[b]	NR	1; 6[a]; 3[b]	NR	2[a, d]; 4[b, d]	NR
Incidental Inhalation-Powder	5; 70[b]	0.0066[c]	2[b]; 3[c]	NR	4[b, d]	NR
Dermal Contact	235	0.0066 - 1	14	NR	9[d]	NR
Deodorant (underarm)	1[a]	NR	NR	NR	NR	NR
Hair - Non-Coloring	137	NR	2	NR	2[d]	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	NR	NR
Mucous Membrane	28	NR	NR	NR	NR	NR
Baby Products	NR	NR	3	NR	NR	NR

	Glycine Soja (Soybean) Flour		Glycine Soja (Soybean) Germ Extract		Glycine Soja (Soybean) Lipids	
Totals*	**66[d]**	**0.0001**	**47[d]**	**0.00002 – 0.45**	**51[d]**	**0.086 – 0.65**
Duration of Use						
Leave-On	*64[d]*	*0.0001*	*40[d]*	*0.0002 – 0.45*	*41[d]*	*0.086 – 0.65*
Rinse-Off	*2[d]*	*NR*	*7[d]*	*0.00002 – 0.00014*	*10[d]*	*NR*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*NR*	*NR*	*NR*
Exposure Type						
Eye Area	1[d]	NR	6[d]	0.01	6[d]	0.09
Incidental Ingestion	NR	NR	NR	NR	2[d]	0.65
Incidental Inhalation-Spray	60[a, d]; 1[b, d]	NR	8[a,d]; 16[b,d]	NR	20[a,d]; 7[b,d]	NR
Incidental Inhalation-Powder	1[b, d]	0.0001[c]	16[b,d]	0.005 – 0.45[c]	1[d]	NR
Dermal Contact	64[d]	0.0001	47[d]	0.00002 – 0.45	43[d]	0.09
Deodorant (underarm)	NR	NR	NR	NR	NR	NR
Hair - Non-Coloring	2[d]	NR	NR	0.00014 – 0.11	5[d]	NR
Hair-Coloring	NR	NR	NR	NR	NR	NR
Nail	NR	NR	NR	NR	1[d]	NR
Mucous Membrane	1[d]	NR	1[d]	NR	2[d]	NR
Baby Products	NR	NR	NR	NR	NR	NR

	Glycine Soja (Soybean) Seed		Glycine Soja (Soybean) Seed Extract	
Totals*	**1[d]**	**NR**	**NR**	**0.000001 – 2**
Duration of Use				
Leave-On	*NR*	*NR*	*NR*	*0.000001 – 2*
Rinse-Off	*1[d]*	*NR*	*NR*	*0.00008 – 0.7*
Diluted for (Bath) Use	*NR*	*NR*	*NR*	*0.0004*
Exposure Type				
Eye Area	NR	NR	NR	NR
Incidental Ingestion	NR	NR	NR	0.0001
Incidental Inhalation-Spray	NR	NR	NR	0.000001; 0.005[a]
Incidental Inhalation-Powder	NR	NR	NR	0.002 – 2[c]
Dermal Contact	1[d]	NR	NR	0.0004 – 2
Deodorant (underarm)	NR	NR	NR	NR
Hair - Non-Coloring	NR	NR	NR	0.000001 – 0.01
Hair-Coloring	NR	NR	NR	NR
Nail	NR	NR	NR	0.001
Mucous Membrane	NR	NR	NR	0.0001 – 0.0004
Baby Products	NR	NR	NR	NR

NR = Not Reported

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

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

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

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

[d] Reported in the VCRP under a non-INCI name and presented here for information purposes.

Table 5. Soy-Derived Ingredients not reported to be in use

Glycine Max (Soybean) Callus Culture
Glycine Max (Soybean) Callus Culture Extract
Glycine Max (Soybean) Callus Extract
Glycine Max (Soybean) Fiber
Glycine Max (Soybean) Flower/Leaf/Stem Juice
Glycine Max (Soybean) Leaf Cell Extract
Glycine Max (Soybean) Leaf Extract
Glycine Max (Soybean) Phytoplacenta Conditioned Media
Glycine Max (Soybean) Pulp
Glycine Max (Soybean) Seedcake Extract
Glycine Max (Soybean) Seedcoat Extract
Glycine Max (Soybean) Seed Powder
Glycine Max (Soybean) Sprout Extract
Glycine Soja (Soybean) Fiber
Glycine Soja (Soybean) Hull
Glycine Soja (Soybean) Phytoplacenta Extract
Glycine Soja (Soybean) Seedcake Extract
Glycine Soja (Soybean) Seed Powder
Glycine Soja (Soybean) Seed Water
Glycine Soja (Soybean) Sprout Extract

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