7291000G – STRIOVER™

Version: 21 - 11/JUN/2020

1. PRODUCT IDENTIFICATION

Trade Name:	STRIOVER™
Manufacturer:	PROVITAL
Responsible for the Safety Assessment:	Lourdes Mayordomo
Tf./Fax:	3493-7192350/7190294
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Kind of Raw Material:	Active Ingredient
Function of the Ingredient (PCPC Inventory):	Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Miscellaneous
Function of the Ingredient (UE Inventory):	Emollient, Skin Conditioning

2. PRODUCT COMPOSITION

Components Breakdown (INCI). Including actives, solvents, preservatives, antioxidants and other additives:

[EU]		CAS	EINECS
Aqua	40 - 60 %	7732-18-5	231-791-2
Glycerin	40 - 60 %	56-81-5	200-289-5
Astragalus Membranaceus Root Extract	1,5 - 2,5 %	94166-93-5	303-391-9
Codonopsis Pilosula Extract	1,5 - 2,5 %	---	---
Preservatives			
Potassium Sorbate	0,2 - 0,3 %	24634-61-5 590-00-1	246-376-1
Sodium Benzoate	0,2 - 0,3 %	532-32-1	208-534-8

PCPC [CTFA]		CAS	EINECS
Water	40 - 60 %	7732-18-5	231-791-2
Glycerin	40 - 60 %	56-81-5	200-289-5
Astragalus Membranaceus Root Extract	1,5 - 2,5 %	94166-93-5	303-391-9
Codonopsis Pilosula Extract	1,5 - 2,5 %	---	---
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Potassium Sorbate	0,2 - 0,3 %	24634-61-5 590-00-1	246-376-1
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3. TOXICOLOGICAL INFORMATION

Data obtained in our own toxicological tests and/or bibliographical research

Animal testing:

This product has not been the subject of animal testing or retesting for cosmetic purposes by or on behalf of this company.

General information:

American Herbal Products Association: Astragalus membranaceus root- Herbs that can be safely consumed when used appropriately (Class 1)

American Herbal Products Association: Codonopsis Pilosula, root - Herb that can be safely consumed when used

appropriately (Class 1).

The CIR Expert Panel concluded that glycerin is safe in the practices of use and concentration described in the Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014, which include the toxicological data.

The following substances have the GRAS status ('Generally Recognized As Safe'): Glycerin (21CFR182.1320)

The CIR Final Report on Safety Assessment of Sodium Benzoate (IJT, 20(S3):23-50, 2001, reopened 06/10) exists and includes all the toxicological data.

The CIR Final Report on Safety Assessment of Potassium Sorbate (JACT 7 (6): 837-80, 1988, confirmed 04/06) exists and includes all the toxicological data.

Classification according to Council of Europe (*):

Not classified

*(1)- Non-recommended ingredients (2)-Ingredients which could not be assessed (3) –Recommended ingredients

Cytotoxicity:

Astragalus membranaceus, root (RTECS No. CJ1682100): ICLo in vitro, human kidney= 5 gm/L/48H.

Skin Irritation:

STRIOVER (Cod. 72910): In vitro skin irritation test. Product tested at 15% and 100%, topically applied on a reconstituted human epidermis. The results showed a viability of 90% in the undiluted product and a viability of 94% at a dose of 15%, therefore under these conditions, the product STRIOVER is classified as NON-IRRITANT at dermal level.

Glycerin (RTECS no. MA8050000): Draize Test in the skin of rabbit, 500 mg, 24h, mild.

Glycerin (50% in water) was not irritating to subjects with dermatitis (n=420) when administered for 20-24h under occlusion. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Skin Sensitization:

STRIOVER (Cod. 72910): In vitro sensitization study h-Clat (human cell line activation test). Product tested at different concentrations and applied to a culture of human monocytes. The results recorded did not show a significant reaction in monocytes, this product is considered NON-SENSITIZING.

Astragalus membranaceous is a popular herbal medicine used to treat allergic diseases in East Asia. A study performed in mice confirned tha anti-allergenic activity of this plant: the oral administration of Astragalus root extract, at a dose of 100 mg/kg, inhibit ethe development of dermatitis induced by DNFB. (Biol. Pharm. Bull. 30(8) 1468-1471, 2007)

In a sensitization study, natural and synthetic glycerin were not sensitizing to white male guinea pigs (n=12). A moisturizer containing glycerin (65.9%) was not sensitizing in a modified Draize test (n=48). There were no reaction during either the induction or challenge phase. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Eye Irritation:

STRIOVER (Cod. 72910): Evaluation of the eye irritation potential from the in vitro "Short Time Exposure" (STE) test. Product tested at 0.05% and at 5%, applied to a monolayer culture of rabbit cornea cells. The results showed an average viability of 94.3% at 5% and an average viability of 99.2% at 0.05%, therefore according to the results obtained and under the experimental conditions adopted, the product STRIOVER is considered NON IRRITANT at ocular level.

Glycerin (RTECS no. MA8050000): Draize Test eye rabbit = 500 mg/24h, mild.

Mutagenicity:

STRIOVER (Cod. 72910): Bacterial Reverse Mutation Assay (Ames Test) using 5 strains of Salmonella typhimurium (TA1535, TA1537, TA98, TA100 and TA102), both in the presence and absence of a metabolic activation system (S -9). The product was tested at 5 concentrations between 0.312 y 5 mg/plate. The results did not show a significant increase in the number of revertants in any of the strains, so under the conditions tested, this product is classified as NON-MUTAGENIC.

Extracts of Astragalus membranaceus root were not mutagenic in a modified Ames test using Salmonella typhimurium TA98 and TA 100. Furthermore, an aqueous extract of this plant was reported to be antimutagenic in that it inhibited benzo-a-pyrene activity in Salmonella typhimurium TA100 (WHO Monographs on selected medicinal plants, Vol 1, pp:56, 1999)

Glycerin was not genotoxic in multiple Ames tests using multiple strains of Salmonella typhimurium up to 50mg/plate. It was not genotoxic in a cytogenetic assay, in a HGPRT assay, sister chromatid exchange assay using

CHO cells, unscheduled DNA synthesis assay using rat hepatocytes, or a in vitro chromosome aberration test using CHO cells, up to 1.0mg/mL was tested in these studies. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Moreover in two in vivo chromosome aberration assays, glycerin was not genotoxic when administered orally to rats at 1mg/kg or by injection into the abdomen at 1000/mg/kg. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Acute toxicity:

Astragalus membranaceus, root extract (RTECS no. CJ1682100): TDLo p.o. human= 300 mg/kg

No adverse effects were observed in mice after oral administration of root of Astragalus at doses up to 100 g/kg, this dose is several hundred times as high as the effective oral dose in humans. (WHO Monographs on selected medicinal plants, Vol 1, pp:55, 1999)

Astragalus membranaceus, root extract (RTECS no. CJ1682100): TDLo p.o. mouse = 20 mg/kg

Astragalus membranaceus root, polysaccharide fraction (RTECS No. CJ1682050): TDLo i.p. mouse= 8 mg/kg.

Codonopsis: DL50 i.p. mice = 79.2 g/kg; Codonopsine: DL50 i.p. mice = 66 a 79 mg/kg. (The Essential Guide to Herbal Safety, 2005, 341-342, ISBN 0443071713)

Codonopsis pilosula (Franch.) Nannf., extract (RTECS Nº GG8370000): LD50, Intraperitoneal, mouse = 7600 mg/kg; LD50, Intravenous, mouse = 1700 mg/kg.

Glycerin (RTECS no. MA8050000): TDLo oral in human = 1428 mg/kg.

Glycerin (RTECS no. MA8050000): LD50 in rat: p.o. = 12600 mg/kg, i.p. = 4420 mg/kg, s.c. = 100 mg/kg, i.v. = 5566 mg/kg. LDLo in rat i.m. = 10 mg/kg, TDLo in rat i.m. = 5 g/kg.

Glycerin (RTECS no. MA8050000): LD50 oral mouse = 4090 mg/kg, LD50 i.p. mouse = 8700 mg/kg, LD50 s.c. mouse = 91 mg/kg, LD50 i.v. mouse = 4250 mg/kg, LD50 oral rabbit = 27 g/kg, LD50 i.v. rabbit = 53 g/kg, TDLo i.m. rat = 4 mL/kg, TDLo i.m. rat = 4000 mg/kg.

Subchronic and chronic toxicity:

Subchronic toxicty study of root of Astragalus membranaceus estract in rats and dogs. These animals were daily administered of product by intra-peritoneum or vein for three months. The product was safe without any distinct toxicity and side effects, the dosage range is 5.7-39.9 g/kg for rataa and 2.85-19.95 g/kg for dogs, which is equal to 70 or 35 times of that of human (0.57 g/kg) respectively. (J Ethnopharmacol. 2007 21;110(2):352-5)

Astragalus membranaceus, root extract (RTECS no. CJ1682100): TDLo p.o. mouse = 2800 mg/kg/10W-I, TDLo p.o. mouse = 3360 mg/kg/12W-I, TDLo p.o. rat = 35000 mg/Kg/7D-C, TDLo i.p. rat = 3630900 mg/kg/91D-I and TDLo i.v. dog = 316680 mg/kg/6W-I, TDLo p.o. mouse = 210 mg/kg/7D-I, TDLo p.o. rat = 56000 mg/kg/8W-I, TDLo i.v. rat = 42 ml/Kg/3W-I and TDLo i.v. mouse = 560 mg/kg/4w-I

Astragalus membranaceus (var. mongholicus), root, etanol extract, flavonoid content (RTECS no. CJ1682030): TDLo p.o. rat = 840 mg/kg/6W-I and TDLo p.o. rat = 4200 mg/kg/6W-I

Astragalus membranaceus, root dried powder (RTECS No. CJ1682027): TDLo p.o. mouse= 126 gm/kg/4W-I.

Astragalus membranaceus root, polysaccharide fraction (RTECS No. CJ1682050): TDLo p.o. mouse= 20 mg/kg/4D-I; TDLo i.p. mouse= 25 mg/kg/5D-I; TDLo i.p. mouse= 35 mg/kg/7D-I; TDLo p.o. rat= 14000 mg/kg/5W-C; TDLo p.o. mouse= 39200 mg/kg/8W-I; TDLo p.o. mouse= 19600 mg/kg/4W-I.

Codonopsis did not produce toxic reactions when administered to rats by subcutaneous injection (0.5g) for 13 days or to rabbits by intraperitoneal injection (1g) for 15 days. (The Essential Guide to Herbal Safety, 2005, 341-342, ISBN 0443071713)

Codonopsis pilosula (Franch.) Nannf., root, aqueous extract (RTECS Nº GG8376000): TDLo, oral, mouse = 126 g/kg/4W.

Glycerin (RTECS no. MA8050000): TDLo oral rat = 96 g/kg/30d-I, TDLo oral mouse = 560 g/kg/8w-C, TDLo oral mouse = 2800 mg/kg/25w-C.

The NOAEL of glycerin in rats was between 115 and 2300 mg/kg when orally administered in water for 44days.The NOEL in dogs was 950 when orally administered for 3 days. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

In repeated dose toxicity studies with humans there were no signs of toxicity or effects on blood or urine production when subjects (n=14) were orally administered glycerin (1.3 - 2.2 g/kg/day) for 50 days.(Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

There were no treatment effects when glycerin (100%; 0.5 - 4mL) was administered to 30% of the body surfaces of rabbits for 45 weeks.(Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

The inhalation NOAEL was 0.167 for glycerin administered nose only for 5h/day, 5day/week for 13 weeks in rats. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Reproductive effects:

STRIOVER (Cod. 72910): This product has not been tested in pregnant women; however, according to the raw materials used and the bibliographic information on the toxicity of its components, there are no contraindications in this use. Therefore, this product can be used in cosmetic products for pregnant women at the recommended dose of use.

A combination of Codonopsis Pilosula and Astragalus was used in a study with pregnant women for the treatment of PIH-induced kidney damage (pregnancy induced hypertension) showing a clear reparative function in patients. (Maternal and Child Health Care of China 2010 Vol. 25 No. 23 pp. 3350-3353)

Astragalus Membranaceus - Pregnancy category B1: No increase in frequency of malformation or other harmful effects on the foetus from limited use in women. No evidence of increased foetal damage in animal studies (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, First edition 2005, pp 249-251).

No adverse effects expected during the use of Astragalus Membranaceus during pregnancy and lactation. (Principles and Practice of Phytotherapy. Modern Herbal Medicine, Simon Mills and Kerry Bone, Churchill Livingstone, 2000, pp 273-279).

Codonopsis Pilosula - Pregnancy category B1: No increase in frequency of malformation or other harmful effects on the foetus from limited use in women. No evidence of increased foetal damage in animal studies (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, First edition 2005, pp 341-342).

The use of Codonopsis Pilosula is compatible with breastfeeding (The Essential Guide to Herbal Safety, Simon Mills and Kerry Bone, Elsevier, First edition 2005, pp 341-342).

In a two-generation reproductive study in rats (n=10/sex), the administration of glycerin (0,20%; 2000mg/kg/day in drinking water) for 8 weeks before mating until weaning of pups produced no adverse effects on the reproductive efficiency of the parents (F0) or the development of the offspring (F1). (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

When glycerin was administered orally to rats and mice on days 6 through 15 of gestation, there were no adverse effects observed in the dams. The NOAEL for maternal toxicity and teratogenicity was 1310 mg/kg/d for rats and 1280 mg/kg/d for mice. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

When glycerin was administered orally to rabbits (n=25) on days 6 through 18 of gestation, there were no adverse effects found in the dams. The NOAEL for maternal toxicity and teratogenicity was 1180 mg/kg/d. (Safety Assessment of Glycerin as Used in Cosmetics, Final Report, December 2014)

Glycerin (RTECS no. MA8050000): rat, i.t. TDL0 = 280 mg/kg, 2 days, male; rat oral TDL0 = 100 mg/kg, 1 day, male; rat, i.t., TDL0 = 862 mg/kg, 1 day, male.

Other data:

STRIOVER (Cod. 72910): The UV-vis absorption spectrum of the STRIOVER was evaluated; in accordance to the established in the OECD protocol No. 101. In the absorption range 400-300nm (UVA), the results show that the product does not absorb, therefore the product STRIOVER does not exhibit phototoxic potential.

4. ECOLOGICAL DATA

Biodegradability:

Glycerin (HSDB no. 492, revision: 20050624): Activated sludge test: 220 mg/l resulted in a COD of 97%; Test in a 5 days: BOD = 82%. Glycerin is considered an easily degradable substance.

Aquatic Toxicity:

Glycerin (HSDB no. 492, revision: 20050624): LC50 goldfish > 5000 mg/l/24h.

Glycerin: Multiplication inhibition test in algae (Microcystis aeruginosa) and protozoa (Entosiphon sulcatum): Toxicity threshold = 2900 mg/l and 3200 mg/l (HSDB no. 492, revision: 20050624).

Other data:

No data available.

5. CONCLUSION

The European cosmetics legislation (Regulation (EC) No 1223/2009) establishes the need to assess the safety of cosmetic products, taking into account the toxicological profile of the ingredients. To do this, in the case of possible systemic effects, it is necessary to obtain the NOAEL (no observed adverse effects level) for the calculation of MoS (margin of safety). The absence of these considerations shall be duly justified.

The NOAEL value, or else other data used for the same purpose (LOAEL, LD50, etc.), can only be calculated experimentally from toxicological studies that require the use of animals. Since Provital does not perform any animal testing, it has established a system to ensure the safety of its products without the need of NOAEL and the subsequent calculation of MoS. This systematic, in the case of natural complex substances (NCS) has been endorsed by international organisms and renowned toxicologists.

The safety of this ingredient is then established based on the following information: known uses of the active in different fields (medicine, food, cosmetics, etc.), profile of the chemical compounds of the ingredient and bibliographic toxicological information available for the active and its components. The integration and study of all these data allows for a conclusion on the safety of the ingredient.

The components of this product have registered adverse effects neither in its described uses nor in the historical marketing of this company. These data and the available toxicological information lead to the conclusion that the use of this product, under the normal conditions of cosmetic use, involves no risk for consumers.

STRIOVER (Cod. 72910): This product has not been tested in pregnant women; however, according to the raw materials used and the bibliographic information on the toxicity of its components, there are no contraindications in this use. Therefore, this product can be used in cosmetic products for pregnant women at the recommended dose of use.