7450000G – HAPPY SKIN

Version: 22 - 24/AUG/2015

1. PRODUCT IDENTIFICATION

Trade Name:	HAPPY SKIN
Manufacturer:	PROVITAL
Responsible for the Safety Assessment:	Lourdes Mayordomo
Tf./Fax:	3493-7192350/7190294
e-mail:	l.mayordomo@provitalgroup.com
Kind of Raw Material:	Active Ingredient
Function of the Ingredient (PCPC Inventory):	Skin Protectants; Skin-Conditioning Agents - Emollient
Function of the Ingredient (UE Inventory):	Skin Protecting; Emollient
INCI approved in:	Registered in EU, USA, Japan
Japanese Name:	JCLS: --- Japanese translation available in PCPC.

2. PRODUCT COMPOSITION

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

[EU]		CAS	EINECS
Glycerin	40 - 60 %	56-81-5	200-289-5
Aqua	40 - 60 %	7732-18-5	231-791-2
Rhodiola Rosea Root Extract	2 - 4 %	92457-37-9	296-320-5
Preservatives			
Phenoxyethanol	0,7 - 0,9 %	122-99-6	204-589-7
Potassium Sorbate	0,2 - 0,4 %	24634-61-5 590-00-1	246-376-1

PCPC [CTFA]		CAS	EINECS
Glycerin	40 - 60 %	56-81-5	200-289-5
Water	40 - 60 %	7732-18-5	231-791-2
Rhodiola Rosea Root Extract	2 - 4 %	---	---
Preservatives			
Phenoxyethanol	0,7 - 0,9 %	122-99-6	204-589-7
Potassium Sorbate	0,2 - 0,4 %	24634-61-5 590-00-1	246-376-1

Impurities:

Heavy Metals (as Pb)	Less than 20 ppm.
Pesticides	No data available. Not expected to be found.

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:

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 Potassium Sorbate (JACT 7 (6): 837-80, 1988, confirmed 04/06) exists and includes all the toxicological data.

There is a CIR Final Report declaring Phenoxyethanol safe for use in cosmetics and including all toxicological data (JACT, 9 (2), 1990; confirmed in IJT-30 (Suppl.5) 2011).

Classification according to Council of Europe (*):

Non-classified.

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

Cytotoxicity:

Rhodiola rosea L., root, 20% ethanol extract, hydrochloric acid hydrolysated (RTECS nºVI9036500): ICLo in vitro, mouse-melanoma= 60ug/mL/24h; 5ug/mL/24h

Rhodiola rosea L., root, 20% ethanol extract (RTECS nºVI9030500): ICLo in vitro, mouse-melanoma= 50ug/mL/24h

Skin Irritation:

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:

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:

HAPPY SKIN (Cod. 7450):In-vitro Irritation Index: HET-CAM (con.100%) :0.75

Test performed with other products of Provital: RHODIOLA COMPLEX (Cod. 42401): The Hen's Eggs Test on the Chorioallantoic Membrane (HET-CAM), product tested at 25%, Mean Irritation Index = 0.75. The trial product can be considered as Practically Non Irritant at the ocular level.

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

Mutagenicity:

Rhodiola extracts has antimutagenic effects in chromosome aberrations and micronuclei test in mouse and in unscheduled DNA test.(Patol.Fiziol.Eksp.Ter.1997(4):22-4)

Ethanolic extracts of Rhodiola showed antimutagenic effects in Salmonella typhimurium TA98 and TA100 (Tsitol Genet.1999,33(6):19-25)

Extracts of Rhodiola rhizomes shows anticancer effects in HL-60 cells (J.Ethnophramacol.2006, 103(1):43-52) and in several tumors in rat and mouse (Vopr Onkol1987;33 (7):57-60)

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:

Rhodiola rosea, extract (RTECS nº VI8980000):LD50 s.c. mouse = 28600 uL/kg

Rhodiola rosea, root (RTECS nº VI9024500):LD50 p.o. rat and mouse > 21500 mg/kg

Rhodiola rosea, estandardized SHR-5 extract (RTECS no. VI9044500):TDLo p.o.human = 5.3 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:

Rhodiola rosea L., root (RTECS nºVI9024500): TDLo p.o. rata = 3600 g/kg/90D-I

Rhodiola rosea L., extract (RTECS nºVI8980000): TDLo p.o. rat= 4mL/kg/10D-I; 21mg/kg/3D-I; 31.5 g/kg/3W-I. TDLo p.o mouse= 4mL/kg/10D-I; 50 mL/kg/10D-I.

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:

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.

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)

Other data:

Clinical trials with acute dose of 1.5-2 g of an Rhodiola extract (with 2% of rosavin) and chronic dose of 180-300 mg/day showed no toxic effects (Alternative Medicine Review 2001,6(3):299-300)

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: 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).

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

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.