4861000G – GREEN TEA - ECO[1]

Version: 23 - 24/AUG/2015

1. PRODUCT IDENTIFICATION

Trade Name:	GREEN TEA - ECO[1]
Manufacturer:	PROVITAL
Responsible for the Safety Assessment:	Lourdes Mayordomo
Tf./Fax:	3493-7192350/7190294
e-mail:	l.mayordomo@weareprovital.com
Kind of Raw Material:	Active Ingredient
Function of the Ingredient (PCPC Inventory):	Antifungal Agents; Antimicrobial Agents; Antioxidants; Cosmetic Astringents; Fragrance Ingredients; Light Stabilizers; Oral Care Agents; Skin Protectants; Skin-Conditioning Agents - Emollient; Skin-Conditioning Agents - Humectant; Skin-Conditioning Agents - Miscellaneous
Function of the Ingredient (UE Inventory):	Antimicrobial, Antioxidant, Astringent, Emollient, Humectant, Masking, Oral Care, Skin Conditioning, Skin Protecting, Tonic, UV Absorber
INCI approved in:	Registered in EU, USA, Japan
Japanese Name:	JCLS :Green Tea Extract 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
Camellia Sinensis Leaf Extract[1]	2 - 5 %	84650-60-2	283-519-7
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
Glycerin	40 - 60 %	56-81-5	200-289-5
Water	40 - 60 %	7732-18-5	231-791-2
Camellia Sinensis Leaf Extract[1]	2 - 5 %	84650-60-2	283-519-7
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

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 different Camellia sinensis-derived ingredients among them, Camellia sinensis Leaf Extract, are safe in the practices of use and concentration described in the safety assessment: Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014, when formulated to be non-sensitizing.

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'): Thea sinensis (21CFR182.20), Caffeine (21CFR182.1180), 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 (*):

Non-classified.

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

Cytotoxicity:

No data available.

Skin Irritation:

Cod. 4861 Patch Test (30 min), IIP =10%, Patch Test (48 h), IP =0%

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)

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

Skin Sensitization:

In a sensitization study a oolong tea extract (1% solids) was not sensitizing to guinea pigs. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

IFRA reported that in a local lymph node assay (LLNA) EC3 was > 1250 ug/cm2 for camellia sinensis leaf extract. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

In various HRIPT with cosmetic products containing leaf extracts of Camellia sinensis (Black tea) it was concluded that those products were not irritant or sensitizing, in one HRIPT the NOAEL was 480ug/cm2. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

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:

Green Tea Eco (Cod. 4861): In-vitro Irritation Index: HET-CAM (con. 100%): 3.54.

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

Mutagenicity:

Camellai sinensis leaf extract was not genotoxic in 2 Ames tests up to 5000 ug/plate. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

Epicatechin (RTECS no. KB3745000): Sister chromatid exchange in human lymphocyte = 500 mg/l; Mutation in Salmonella typhimurium = 5 µmol/plate/48h.

Epigallocatechin-3-gallate (RTECS no. KB5200000): DNA damage in human lymphocyte = 0.02 mmol/l/10M.

Fractions of tannic acid in Camellia sinensis (Indian J Exp Biol 1991 May; 29(5): 401-6): No mutagenic activity in

AmesTest in strains TA98, TA100, TA 1535 and TA1538, with or without metabolic activation.
Catechin: Human lymphocyte tests: UDS 200 µg/l and inhibition of DNA synthesis 13 mg/l (ARZNAD 35, 1209, 85); chromatid exchange 5 µmol/l (CNREA 8 45, 2471, 85).
Catechin: DNA repair E.coli, 4500 µmol/l (MUREAV 272, 145, 92); effects on human lymphocyte chromosome, 500 mg/l (MUREAV 246, 205, 91).
Epigallocatechin (RTECS no. KB5100000): DNA inhibition in microorganism = 400 mg/l, 100 mg/l; DNA inhibition in HeLa cells = 25 mg/l.
Camellia sinensis, leaf (green tea), water extract, 33.1% total catechins (RTECS no. EW9796000): Cytogenetic analysis in hamster lung = 266.7 mg/l/6h, mutation in somatic cells of mouse = 1055 and 2250 mg/l/3h.
Camellia sinensis leaf (green tea), water extract, 63.7% total catechins preparation (RTECS no. EW9797000): Cytogenetic analysis in hamster lung = 287 mg/l/6h and 358 mg/l/6h, Mutation in somatic sells of mouse = 722 mg/l/3h and 1000 mg/l/3h.
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:

Oral acute toxicity studies were carried out in rats with leaf extracts of green and black tea, the minimum lethal dose was >2 g/kg, there were no effects on weight gains and there were no mortalities. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)
The oral LD50 of a Chinese tea extract (0.85% solids) and a oolong tea extract (1% solids) was >2 g/kg for mice, and the oral LD50 of a green tea extract (1,6% solids) was >2 L/kg for rats. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)
Catechin (RTECS no. DJ3450000): LD50 (g/kg): p.o. rat > 10, s.c. rat > 5, i.v. rat > 0.1, p.o. mouse > 10, s.c. mouse > 5, i.v. mouse > 0.1, i.p. rat =1.084; TDLo mouse skin >40 mg/kg.
Camelia sinensis Extract: LD50 p.o. (mouse) = 3900 mg/kg (CTYAD 8 12, 173, 81); LD50 i.p. (mouse) = 316 mg/kg (IJEBA 6 26, 883, 88).
Epigallocatechin-3-gallate (RTECS no. KB5200000): TDLo i.p. rat = 40 mg/kg, guinea pig subcutaneus = 25 mg/kg and rabbit intravenous = 1mg/kg; LD50 rat skin > 1860 mg/kg; LD p.o. rat = 2000 mg/kg; TDLo p.o. dog = 120 mg/kg; LDLo s.c. rat = 500 mg/kg.
Camellia sinensis leaf extract (RTECS EW9800000): TDLo ip mouse = 464 mg/kg.
Epicatechin (RTECS no. KB3745000): LD50 i.p. mouse = 1 g/kg, TDLo i.v. rat = 30 µg/kg.
Camellia sinensis, leaf (green tea), water extract, polyphenolic fraction (RTECS no. EW9801160): TDLo p.o. rat = 100 mg/kg.
Camellia sinensis (green tea), dried powder, suspension in saline at room temperature (RTECS no. EW9794000): TDLo p.o. mouse = 300 mg/kg.
Camellia sinensis (green tea), dried powder, hot water suspension (RTECS no. EW9793000): TDLo oral human = 21.4 mg/kg.
Camellia sinensis var. sinensis, saponin (RTECS no. EX0220000): LDLo p.o. mouse = 1 g/kg.
Camellia sinensis, fresh tea leaves, hot water extract (RTECS no. EW9795000): TDLo s.c mouse = 300 mg/kg.
Epigallocatechin-3-gallate (RTECS no. KB5200000): LD50 p.o. mouse = 2170 mg/kg; TDLo p.o.mouse = 25 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:

Epigallocatechin-3-gallate (RTECS no. KB5200000): TDLo mouse: p.o. = 16.8 g/kg/12w-C, p.o. = 50 mg/kg/2d-I, i.p. = 175 and 350 mg/kg/7d-I, skin = 7200 mg/kg/12w-I; rat i.p. = 70 mg/kg/7d-I.

Epigallocatechin-3-gallate (RTECS no. KB5200000): TDLo p.o. mouse = 4539.6 mg/kg/90d-C; administration onto skin of guinea pig = 10 pph/17d-I and 5 pph/22d-I; oral in dog = 12000 mg/kg/30d-I, 3600 mg/kg/9d-I and 36400 mg/kg/13w-I; subcutaneus in rat = 2400 mg/kg/12d-I.

Catechin (RTECS no. DJ3450000): TDLo i.p. rat = 800 mg/kg/4w-I, i.p. mouse = 90 mg/kg/9d-I, p.o. mouse = 400 mg/kg/10d-I.

Epicatechin (RTECS KB3745000): TDLo i.p. rat = 525 mg/kg/5w-I.

Camellia sinensis leaf extract (RTECS EW9800000): TDLo p.o. rat = 2016 mg/kg/3d-I.

Green tea, commercial extract, 91% epigallocatechin gallate (RTECS no. ME2470000): TDLo p.o. rat = 42000 mg/kg/10w-C.

Camellia sinensis leaf (green tea) catechins (RTECS no. WT9830000): TDLo p.o. rat = 24.732 g/kg/1w-C, TDLo p.o. rat = 16.191 g/kg/90d-C, TDLo p.o. rat = 16.965 g/kg/90d-C, TDLo p.o. rat = 68.751 g/kg/90d-C, TDLo p.o. rat = 71.280 g/kg/90d-C, TDLo p.o. rat = 3533 g/kg/90d-C.

Camellia sinensis leaf (green tea), water extract (RTECS no. EW9801220): TDLo p.o. rat = 1400 ml/kg/7d-I, TDLo oral human = 0.07 g/kg/4w-I, TDLo p.o. rat = 8400 mg/kg/4w-I, TDLo p.o. mouse = 252000 mg/kg/12w-C, TDLo p.o.mouse = 37100000 mg/kg/25w-C, TDLo p.o. mouse = 3584000 mg/kg/4w-C, TDLo p.o. mouse = 168000 mg/kg/20w-C, TDLo p.o. mouse = 26000 mg/kg/52d-C, TDLo p.o. rat = 700 mg/kg/7d-I, TDLo p.o. rat = 22500 mg/kg/15d-C, TDLo oral human = 41683 ml/kg/20y-I.

Camellia sinensis, leaf (green tea), water extract, 33.1% total catechins (RTECS no. EW9796000): TDLo oral rat = 28000 mg/kg/28d-I, TDLo p.o. rat = 14000 mg/kg/7d-I, TDLo p.o. rat = 56000 mg/kg/28d-I, TDLo p.o. rat = 7200 mg/kg/12d-I.

Camellia sinensis, leaf (green tea), water extract, polyphenolic fraction (RTECS no. EW9801160): TDLo p.o. rat = 900 mg/kg/18d-I, TDLo p.o. rat = 750 mg/kg/15d-I, TDLo p.o. rat = 1500 mg/kg/15d-I, TDLo p.o mouse = 3000 mg/kg/5w-I.

Camellia sinensis (green tea), 70% ethanol extract (RTECS no. EW9792000): TDLo p.o. mouse = 119 mg/kg/7d-I.

Camellia sinensis leaf (green tea) catechins (RTECS no. WT9820000): TDLo p.o. rat = 59690.4 mg/kg/24w-C.

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:

In a reproductive and developmental toxicity study there were no adverse effects when pregnant rats (n=6) were orally administered camellia leaf extract up to 1366 mg/mL/day. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

Catechin: Test on rat, p.o.: fetotoxicity TDLo = 55 g/kg (7-17d preg), viability index TDLo = 1.2 g/kg (17-22d preg/21d post) (OYYAA2 24, 495, 82).

Epigallocatechin-3-gallate (RTECS no. KB5200000): TDLo p.o. rat = 1000 mg/kg (multigenerational) and 161 g/kg.

Green tea, commercial extract, 91% epigallocatechin gallate (RTECS no. ME2470000): TDLo p.o. rat = 27.7 and 92.4 g/kg, male and female 10 weeks pre-mating.

Camellia sinensis, leaf (green tea), water extract, 33.1% total catechins (RTECS no. EW9796000): TDLo p.o. rat = 7200 mg/kg, female 6-17 days after conception.

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:

In a phototoxicity study, there were no signs of erythema on treated sites on the forearms of subjects (n=6) treated with camellia sinensis leaf extracts (10% in form of green or black tea) and exposed to UVA, B, C. (CIR Final Report, Safety Assessment of Camellia sinensis-Derived Ingredients as Used in Cosmetics, October 15, 2014)

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.

local laws. Provital does not guarantee efficacy experimental results under conditions other than those specified. Provital also reserves the right to make changes to this document due to technical progress or further developments.