7251000G – PROVISLIM™

Version: 23 - 24/AUG/2015

1. PRODUCT IDENTIFICATION

Trade Name:	PROVISLIM™
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):	Fragance Ingredients; Skin-Conditioning Agents - Miscellaneous
Function of the Ingredient (UE Inventory):	----, Masking, Perfuming, Skin Conditioning
INCI approved in:	Registered in EU, USA, Japan
Japanese Name:	JCLS: --- Raspberry Ketone: Japanese translation available in PCPC. Provislim has been registered in Japan.

2. PRODUCT COMPOSITION

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

[EU]		CAS	EINECS
Propanediol	85 - 95 %	504-63-2 26264-14-2	207-997-3
Aqua	5 - 15 %	7732-18-5	231-791-2
Fisetin	1 - 1,3 %	528-48-3	208-434-4
Raspberry Ketone	0,8 - 1,1 %	5471-51-2	226-806-4
Preservatives			
none	0 %	---	---

PCPC [CTFA]		CAS	EINECS
Propanediol	85 - 95 %	504-63-2 26264-14-2	207-997-3
Water	5 - 15 %	7732-18-5	231-791-2
Fisetin	1 - 1,3 %	528-48-3	208-434-4
Raspberry Ketone	0,8 - 1,1 %	5471-51-2	226-806-4
Preservatives			
none	0 %	---	---

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 following substances are used as Food Additives permitted for human consume by FDA: Raspberry Ketone: 4-(p-Hydroxyphenyl)-2-butanone (21 CFR172.515)

Classification according to Council of Europe (*):

Not classified

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

Cytotoxicity:

PROVISLIM (Cod. 72510): Neutral Red Release Assay performed using SIRC cell line. Results: CI50>50%, % of mortality at dilution 50% = 24%. Unimportant cytotoxicity.

Skin Irritation:

PROVISLIM (Cod.72510): Patch Test on 10 volunteers, occlusive patch for 48 hours, product tested at 25%. No irritant reactions were registered at 15 minutes and 24 hours after patch removal. The clinical cutaneous compatibility of this product may be judged "Very Good"

Propanediol (RTECS no. TY2010000, Last Updated:200608): Standard Draize Test in human skin, product at 100% for 48 hours and 7 days, moderate

Propanediol. Skin irritation tests in NZW rabbit: undiluted product at 0.5ml was considered to be a Slight irritant. (Supplier data)

Skin Sensitization:

PROVISLIM (Cod. 72510). Marzulli and Maibach's Method: Human Repeated Insult Patch Test. Product tested at 25%. No pathological irritation, nor sensitisation reaction was registered. Provislim is classified as a No-Sensitizant product.

Propanediol. Skin sensitization tests: Studies performed in guinea pigs by Landsteiner/Draize method and by Magnusson-Kligman method considered the product to be non-sensitizing. Studies in human at product concentration of 50% in 112 volunteers and 75% in 207 volunteers considered the product not to be a primary skin irritant or a sensitizing agent. (Supplier data)

Eye Irritation:

PROVISLIM (Cod. 72510): Bovine Cornea Opacity and Permeability Test (BCOP), product tested at 25%. Corneal score at 30 min =1.4, Corneal score at 4h = 24.5. This product is classified as Weakly Irritant.

Propanediol. Eye irritation tests in NZW rabbit: undiluted product at 0.1ml was considered to be Non-irritating and at 0.2 ml was considered to be Practically non-irritating. (Supplier data)

Mutagenicity:

PROVISLIM (Cod. 72510): Comet Assay performed in a cell suspension of human keratinocytes (HaCat). The product was tested at the following doses: 333, 111, 37, 12, 4 and 1 ug/ml. It showed a % of DNA in the tail equivalent to the control culture and it was classified as a Non Genotoxic Substance. By other hand, PROVISLIM at doses of 2.6, 5.6 and 12 ug/ml showed a protective effect against the genotoxic activity of hydrogen peroxide.

Propanediol. Genetic toxicity tests: This product was considered non-mutagenic in the Ames Test (OECD method no.471), in the HPRT Test (OECD method no. 476), in the chromosome aberrations test (OECD method no.473) and in the in vivo mouse micronucleus test (92/69/EEC Method) (Supplier data)

Acute toxicity:

Fisetin (RTECS nº LK9250000): LD50 i.v. mouse = 180 mg/kg

Raspberry Ketone (RTECS no. EL8925000): LD50 p.o. rat = 1320 mg/kg, LD50 i.p. rat = 350 mg/kg

Propanediol (RTECS no.TY2010000, Last Updated:200608): LDLo p.o rat = 10g/kg, LDLo i.m. rat = 6 g/kg, LD50 i.p. mice = 4780 mg/kg, LDLo p.o cat = 3 g/kg, LDLo i.v. rabbit = 3 g/kg, LD50 p.o mice = 4500 mg/kg

Propanediol. Acute toxicity tests: p.o. in rat LD50 = 15800 mg/kg, dermal in rat LD50 > 4200 mg/kg and inhalation in rat, DL > 5000 mg/m3. (Supplier data)

Subchronic and chronic toxicity:

Raspberry ketone: NOEL = 280 mg/kg/d in a 13-week study in rats (WHO Food Additives Series 46)

Propanediol. Repeat-Dose Toxicity tests: p.o. in rat for 90 days NOEL = 1000 mg/kg/day and inhalation in rat after 9 exposures NOEL= 1800 mg/m3. (Supplier data)

Reproductive effects:

Propanediol. Prenatal development toxicity test in rat (OECD method no. 414), the product administered at 250 and 1000 mg/kg by oral gavage on gestation days 6-15, was considered non-toxic. Study on effects during reproduction in rats after a 90-day oral administration, there were no effects to reproductive organs and

differences in fertility. (Supplier data)

Other data:

There are numerous studies that shows anticarcinogenic effects of fisetin. It was demonstrated that fisetin inhibits the metastasis of prostate cancer PC-3 cells (Mol Cell Biochem. 2010 Jan;333(1-2):169-80), of the human lung cancer cell line A549 (J Agric Food Chem. 2009 Oct 14;57(19):8933-41), human pancreatic cancer AsPC-1 cells (Int J Cancer. 2009 Nov 15;125(10):2465-73) and the SNU-C4 colorectal and MDA-MB-231 breast adenocarcinoma cells (Biol. Pharm. Bull. 2008 31(2) 255:259).

4. ECOLOGICAL DATA

Biodegradability:

Propanediol: BOD5 = 1160000 mg/L (Supplier data)

Aquatic Toxicity:

Propanediol. Acute toxicity tests: Fish (Pimephales promelas) LC50 = 7417 mg/L, Daphnia magna EC50 = 7417 mg/L and growth inhibition of algae EC50 > 10000 mg/L (Supplier data)

Other data:

No data available.

5. CONCLUSION

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.