Final Report 2012/1463 INCi

TOXICOLOGICAL EVALUATION ON UR FOG CARTRIDGE

Study program: 2012/1463 INCi

Contract n: PPR12012020701

Sponsor: UR FOG SRL
VIA GIACINTO COLLEGNO,11
10143 TORINO

Test item: UR FOG CARTRIDGE

Study Director: .....
(Paolo Pescio)

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SUMMARY
A toxicological evaluation of the product "UR FOG CARTRIDGE" connected to its use was performed.
A bibliographical evaluation of the potential skin irritating, sensitizing, ocular and inhalation effects of the compounds of test item was carried out.

INTRODUCTION
On behalf of UR FOG SRL, a toxicological evaluation of the item "UR FOG CARTRIDGE" was performed.

The study was performed at the Test Facility Eurofins Biolab S.r.l. of Vimodrone (MI) – via B. Buozzi n. 2 (Italy).

EXPERIMENTATION	*START*	*END*	*RESEARCHER*
Toxicological evaluation	31/08/2012	06/09/2012	Chiara Picotti

BIBLIOGRAPHY

[1] "NTP Technical Report on the toxicology and carcinogenesis studies of dipropylene glycol in F344/N rats and B6C3F$_1$ mice", NTP TR 511, June 2004

[2] TOXNET HDBS DYPROPILENE GLYCOL

[3] Haddock NF, Wilkin JK., "Cutaneous reactions to lower aliphatic alcohols before and during disulfiram therapy", Archives of Dermatology, 1982 Mar;118(3):157-9

[4] http://ntp.niehs.nih.gov/index.cfm?objectid=E881E00B-BDB5-82F8-FBF1562C39F81BA7

[5] TOXNET HDBS ETHYL ALCOHOL

[6] Fruijtier-Pölloth C, "Safety assessment on polyethylene glycols (PEGs) and their derivatives as used in cosmetic products", Toxicology. 2005, Oct 15; 214(1-2):1-38

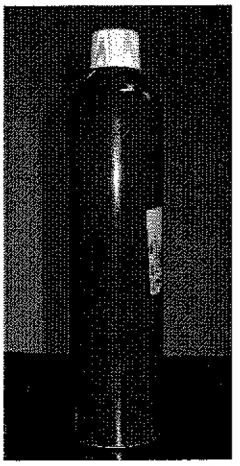
[7] TOXNET POLYETHYLENE GLYCOL – Non human toxicity values

FILING
The study program, all raw data are filed in the archives of Eurofins Biolab S.r.L for ten years after the issuing of the final report.
At the end of the conservation period, the Sponsor may request an extension of the conservation of all or part of the products for a further period, or their restitution. A suitable agreement shall be drafted in this case.

PROCEDURES
All procedures used during this study are recorded in the Eurofins Biolab S.r,L Procedures Manual.

TEST ITEM

The test item consists of a fog fluid contained in a cylinder under CO_2-pressure.



Picture of the test item

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As declared by the Sponsor one cylinder of "UR FOG CARTRIDGE" contains 600 ml of fog fluid.
The volume and weight of ingredients contained in one cylinder are reported in the table below:

[redacted]

In a room of 50 m^2 (approximately 150 m^3), the Sponsor suggests to use "UG FOG CARTRIDGE" for 5 seconds; this application corresponds to 1/6 of the content of one cylinder.
The volume and weight of ingredients released in 150 m^3 are reported in the table below:

[redacted]

The potential routes of exposure in relation with the intended use of the product are: skin contact, ingestion, ocular contact and inhalation.

It's not possible to predict the human assumption of the single ingredients through different routes of exposure; however it can be supposed that the assumed quantity is a fraction of the whole quantity discharged in approximately 150 m^3.
The scope of the device is to stop burglars: the exposure time is very low, limited maximum to few minutes.

A bibliographical evaluation of the potential skin irritating, sensitizing, oral, ocular and inhalation effects of compounds of the test item was carried out.

Each compound was evaluated alone; the interaction between components was not evaluated.

DIPROPYLENE GLYCOL (CASRN: 25265-71-8)

The National Toxicology Program (NTP) performed a toxicological evaluation and a carcinogenesis study about dipropylene glycol.[1]

In the Technical reports on experimental animals and humans results of different scientific articles are reported.

Skin irritating and sensitizing effects
In experimental animals, dipropylene glycol was considered not acutely toxic by dermal exposure.
No mortality occurred when dipropylene glycol was administered to the skin of rabbits at doses of 5 g/kg or 20 mL/kg (20.5 mg/kg).
A formulation containing 7.2% dipropylene glycol produced a cutaneous LD50 greater than 2 g/kg in rabbits.

Dipropylene glycol is only slightly irritating to the skin of rabbits
Ten applications of dipropylene glycol to the skin of rabbits in 12 days produced negligible irritation.
Dipropylene glycol was reported to cause only mild skin irritation in rabbits exposed to 500 mg in a 24-hour dermal application test.

Dipropylene glycol does not produce allergic skin reactions or sensitization in humans. It did not produce irritation in human subjects after a 48-hour closed patch test when administered at a concentration of 20% in petrolatum.

Dipropylene glycol did not produce allergic skin reactions in 503 human volunteers with eczema tested for sensitivity to dipropylene glycol. Patients were exposed to 10% dipropylene glycol for 2 days. Only one patient had a positive patch test reaction to dipropylene glycol.

In a 48-hour closed patch test using a shaving preparation containing 7.2% dipropylene glycol, mild irritation was observed in 6 of 101 subjects after the first exposure and in 8 of 101 subjects after repeating the application 2 weeks later.

Repeated applications of the shaving preparation did not have a sensitizing effect in 50 volunteers treated occlusively for 24 or 48 hours, 3 times per week over a 3-week period. No photosensitizing properties could be detected after ultraviolet irradiation. Likewise, no effects were observed in 59 patients exposed to the shaving preparation for a 4-week period.

The repeated application of a 20% formulation of dipropylene glycol in petrolatum did not have a sensitizing effect on 25 human volunteers.
Exposure to dipropylene glycol consisted of five consecutive treatments, each lasting 48 hours; another 48-hour repeat treatment occurred 1 to 14 days after the fifth consecutive treatment.

Oral effects
In experimental animals, dipropylene glycol was considered not acutely toxic by oral exposure.
The acute oral LD50 value for this substance in rats is approximately 15 g/kg.

Ocular effects
Dipropylene glycol is only slightly irritating to the eyes of rabbits.
In the eyes of rabbits, 510 mg undiluted dipropylene glycol caused irritation and a formulation containing 7.2% produced minimal transient eye irritation.

Inhalation effects
In experimental animals, dipropylene glycol was considered not acutely toxic by inhalation exposure.

Covered 48 hours application of a 50% solution of dipropylene glycol (DiPG) with an unspecified solvent caused irritation in 14 of 34 persons and was equivocally irritant in a further 17. No local effects were induced when 20% DiPG in petrolatum was in 48 hours covered contact with the skin of an unspecified number of volunteers.

No untoward effects have been reported from use of dipropylene glycol nor would any be expected. [2]
Exposure of workers to an emulsion oil containing 4% dipropylene glycol resulted in eye irritation. (However, at least one of the other components present in the oil, methyl isobutyl carbinol, is a known eye irritant; no concentration value). [2]

Dipropylene glycol showed no sensitization reactions in a maximization test that was carried out on 25 volunteers. [2]

AQUA

Aqua was not evaluated.

ETHYL ALCOHOL (CASRN: 64-17-5)

Skin irritating and sensitizing effects
Cutaneous reactions to ethyl alcohol (ethanol), N-propyl alcohol (1-propanol), isopropyl alcohol (2-propanol), and acetaldehyde were evaluated by Haddock NF. et al. in a control group and in patients before and while they were receiving disulfiram therapy. [3]
Local cutaneous erythema was observed from patch tests with ethyl alcohol, N-propyl alcohol, and isopropyl alcohol in hydrated skin, and from acetaldehyde in dry skin. Erythema resulting from topically applied alcohols occurred in a dose-related manner and was caused by a direct vasodilatory effect on the cutaneous microvasculature.

Potential skin irritating effects of ethyl alcohol were investigated by Bingham E. et al. [4]
Human subjects reported no apparent skin irritation when ethanol was applied to the forearm of human subjects in a modified Draize test. No irritation was noted when ethanol was applied to the forearm openly for 21 days, whereas 21-day occlusive test caused erythema and induration toward the end of the exposure period. There have been infrequent reports of skin sensitization reactions attributed to ethanol. Ethanol is a weak sensitizer in a patch test.
Non-human toxicity values are reported below.

- LD50 Mouse subcutaneous 8285 mg/kg [5]
- LDLo Dog subcutaneous: 6600 mg/kg [6]

Ethyl alcohol was considered mildly toxic by skin contact.[6]

Oral effects
Falk M. et al. administered orally to rats by means an intragastric tube ethanol (0.6 g/100 g) in order to evaluate potential toxic effects of this alcohol. [4]
The administration caused an accumulation of secretory vesicles laden with very low density lipoprotein (VLDL) particles which were seen 90 min after administration and later disappeared.

Pankov et al performed a single ethanol oral administration in rats. [4]
In response to alcohol administration the catecholamine secretion from the adrenal medulla was enhanced as evaluated by urinary catecholamine excretion in rats. The threshold dose of 87 mmol/kg also produced a transient increase of blood sugar concentration. Experiments with chronic ethanol treated rats showed that the increase of urinary catecholamine excretion following 87 mmol/kg disappeared occasionally, whereas the increase following repeated administration of 130 mmol/kg is permanent. Morphologic evaluation revealed enlargement of the adrenal medulla, changes of cells and nuclei as well as a distinct reduction of chromaffin reaction.

Non-human toxicity values of LD50 are reported below.

- LD50 Mouse oral: 3450 mg/kg
- LD50 Rat oral: 7060 mg/kg
- LD50 Rat (young) oral: 10.6 g/kg
- LD50 Rat oral: 9.9 g/kg
- LD50 Rat (young adult) oral: 17.8 g/kg
- LD50 Rat (14 days old) oral: 6.2 g/kg
- LD50 Rat (older adults) oral: 11.5 g/kg
- LD50 Dog oral: 5.5 g/kg [5]
- LDLo Dog oral: 5500 mg/kg [6]

Human toxicity values are reported below: [6]

- LDLo Infant (0-1 year) subcutaneous: 7060 mg/kg
- LDLo Human oral: 1400 mg/kg
- LDLo Child (1-13 years): 2000 mg/kg
- TDLo Man oral: 1430 µg/kg
- TDLo Man oral: 50 mg/kg (gastrointestinal tract effects: diarrhea, constipation, ulceration)
- TDLo Man oral: 700 mg/kg
- TDLo Woman oral: 256 g/kg/12 weeks

Ocular effects
Grant et al. treated rabbit eyes with a drop full-strength.[4]
The treatment caused reversible injury graded only 3 on a scale of 10 after 24 hour. Application of 70% alcohol to rabbit corneas injures and temporarily loosens the corneal epithelium, but the recovery was complete. Repeated applications (7 drops) of 40 to 80% alcohol to rabbit eyes over an unspecified but presumably longer time caused loss of corneal epithelium and endothelium, followed by hemorrhages in the conjunctiva, and infiltration and vascularizarion of the corneal stroma.

Inhalation effects
The effects of inhalation exposure of ethyl alcohol were analysed by Bingham E.et al. [4]
In a nontolerant human subject, inhalation exposure to 1380 ppm ethanol for 39 min resulted in no effects at 28 min, but headaches and slight numbness after 33 min. At 3340 ppm for 100 min, sensations of warmth and coldness, nasal irritation, headaches, and numbness were reported. When exposed to 8840 ppm for 64 min, the subjects complained of momentary intolerable odor and difficulty in breathing, conjunctival and nasal irritation, a feeling of warmth, headache, drowsiness, and fatigue. In tolerant individuals, the symptoms are less severe, and the time required to produce them is greater than in intolerant individuals. For instance, a human subject tolerant to alcohol reported slight headaches after 20 min exposure to 5030 ppm for 120 /minutes/. Intoxication has been seen among humans subjected to inhalation of vapors from hot alcohol.

In a study reported by W.M. Grant, alcohol vapor exposure at sufficiently high concentrations may cause prompt stinging and watering of the eyes, but there appear to be no reports of eye injury from industrial exposure to alcohol vapors. [4]
Human volunteers exposed to alcohol vapor have observed at concentrations of 0.7 to 1% vapor in air the smell of alcohol was at first almost unbearable, although unpleasant later, and that the eyes began to burn with increased intensity after several min. A vapor concentration of 0.25% had no notable effect on the eyes.

Non-human toxicity values are reported below.[5]

- LC50 Rat inhalation: 20000 ppm/ 10 hour
- LC50 Mouse inhalation: 39 mg/cu m/4 hour

POLYETHYLENE GLYCOL 200 (CASRN: 25322-68-3)

Skin irritating and sensitizing effects
PEG and its derivatives were analysed in [6]
As regards sensitizing effects, the report observed that only few cases of sensitization reactions caused by PEG and PEG derivatives have been published, mainly involving patients with exposure to PEGs in medicines or following exposure to injured or chronically inflamed skin.
The author reported that on healthy skin, the sensitizing potential of these compounds appears to be negligible and that no safety concern with regard to these endpoints could be identified.
Based on the available data the safety assessment concluded that PEGs of a wide molecular weight range (200 to over 10,000), their ethers, and fatty acid esters, are safe for use in cosmetics.

Animal toxicity data for PEG-200 are reported below: [7]

- LD50 Mouse oral: 3400 mg/kg
- LD50 Rabbit oral: 19900 mg/kg
- LD50 Rat oral: 28000 mg/kg

Osol A. et al. observed that there was no evidence of irritation from base containing 50% polyethylene glycol when applied to either diseased or normal skin of 86 clinical dermatologic patients.[7]

Rowe RC. Et al. affirmed that polyethylene glycols administered topically may cause stinging, especially when applied to mucous membranes. [7]
Hypersensitivity reactions to polyethylene glycols applied topically have also been reported, including urticaria and delayed allergic reactions.

Considering the exposure time and the toxicity of single ingredients, the device pose a low systemic risk to human being if used according to manufacture's instruction. Possible local effects such eye irritation could be considered as transient.