EUROPEAN COMMISSION

Health & Consumer Protection
Directorate-General

Scientific Committee on Consumer Products

SCCP

OPINION ON

1-Naphthol

COLIPA n° A17

Scientific Committees
on consumer products
on emerging and newly identified health risks
on health and environmental risks

The SCCP adopted this opinion at its 15th plenary of 15 April 2008

About the Scientific Committees
Three independent non-food Scientific Committees provide the Commission with the scientific advice it needs when preparing policy and proposals relating to consumer safety, public health and the environment. The Committees also draw the Commission's attention to the new or emerging problems which may pose an actual or potential threat.

They are: the Scientific Committee on Consumer Products (SCCP), the Scientific Committee on Health and Environmental Risks (SCHER) and the Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) and are made up of external experts.

In addition, the Commission relies upon the work of the European Food Safety Authority (EFSA), the European Medicines Evaluation Agency (EMEA), the European Centre for Disease prevention and Control (ECDC) and the European Chemicals Agency (ECHA).

SCCP
Questions concerning the safety of consumer products (non-food products intended for the consumer).
In particular, the Committee addresses questions related to the safety and allergenic properties of cosmetic products and ingredients with respect to their impact on consumer health, toys, textiles, clothing, personal care products, domestic products such as detergents and consumer services such as tattooing.

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1. BACKGROUND

Submission I for 1-naphthol was submitted in May 1983 by COLIPA[1, 2].

The Scientific Committee on Cosmetology (SCC) expressed its opinion at the 48th plenary meeting of 4 October 1991 with the conclusion that *"the use of 1-naphthol in the oxidative hair dyes does not appear to present any health risk."*

The SCC expressed a second opinion at the 54th plenary meeting of 10 December 1993 with the conclusion that *"the SCC requires cutaneous absorption study in more realistic experimental conditions."* The margin of safety was calculated as 3 based on NOAEL of 20 mg/kg bw in a single dose level 90 day study and absorption of 65%.

Submission II for this substance was submitted in July 1996 by COLIPA. The Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP) adopted in the plenary session of 23 June 1999 the opinion SCCNFP/0130/99 with the conclusion, that *"The SCCNFP is of the opinion that 1-Hydroxy-naphthalene can be used safely in permanent hair dye formulations at a maximum concentration of 1.0%. Since permanent hair dyes are mixed with hydrogen peroxide before application, the in-use concentration is 0.5%. The sensitisation data in the dossier was generated with a method not conforming to OECD n° 406. However, no further sensitisation data are requested provided that cosmetic products containing this substance carry a label warning of a risk of sensitisation."*

The substance is currently regulated as an oxidative hair dye by the Cosmetics Directive (76/768/EC), Annex III, part 1 under entry 16 on the List of substances, which cosmetic products must not contain except subject to restrictions and conditions laid down, at a concentration up to 0.5%.

According to the submission III, submitted by COLIPA in September 2005, 1-naphthol is proposed to be used in an oxidative hair product at a concentration up to a maximum level of 4% (2% on-head level).

Submission III presents updated scientific data on the above mentioned substance in line with the second step of the strategy for the evaluation of hair dyes (http://europa.eu.int/comm/enterprise/cosmetics/doc/hairdyestrategyinternet.pdf) within the framework of the Cosmetics Directive 76/768/EEC.

2. TERMS OF REFERENCE

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 1-naphthol safe for use as an oxidative hair dye with a concentration on-head of maximum 2.0% taking into account the scientific data provided?*

2. *Does the SCCP recommend any restrictions with regard to the use of 1-naphthol in oxidative hair dye formulations?*

[1] COLIPA - European Cosmetics Toiletry and Perfumery Association
[2] According to records of COLIPA

3. OPINION

3.1. Chemical and Physical Specifications

3.1.1. Chemical identity

3.1.1.1. Primary name and/or INCI name

1-Naphthol (INCI)

3.1.1.2. Chemical names

1-Hydroxynaphthalene
1-Naphthalenol
Alpha-naphthol
1-Naphthyl alcohol

3.1.1.3. Trade names and abbreviations

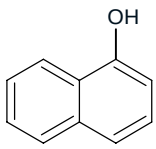
Oxidation base 33
Colorex 1NAP
Jarocol AN
Rodol ERN

CI 76605
COLIPA n° A17

3.1.1.4. CAS / EINECS number

CAS: 90-15-3
EINECS: 201-969-4

3.1.1.5. Structural formula



3.1.1.6. Empirical formula

Formula: $C_{10}H_8O$

3.1.2. Physical form

Off white to light brown flakes

3.1.3. Molecular weight

Molecular weight: 144.17 g/mol

3.1.4. Purity, composition and substance codes

General
Identification by IR, NMR and elemental analysis
Purity: > 99% by HPLC using external standard

Batch n° 138110
Identification by NMR, FTIR and elemental analysis
Purity: 100% by HPLC (290 nm) using Reference Standard (1-naphthol) of 100% purity from Sigma Aldrich

Batch n° BTS0704/01 and BTS0704/02
Purity: > 99.5% (chromatography)
> 99.7% (titration)

Batch n° BTS704/03
Purity: 99.9% (chromatography)

3.1.5. Impurities / accompanying contaminants

General

1-naphthylamine:	< 100 ppm
2-naphthol:	< 1500 ppm
1,6-dihydroxynaphthalene:	< 100 ppm
1,7-dihydroxynaphthalene:	< 200 ppm

Arsenic:	< 5 ppm
Antimony:	< 5 ppm
Lead:	< 20 ppm
Cadmium:	< 10 ppm
Mercury:	< 5 ppm
Loss on Drying:	< 1 %
Residue on Ignition:	< 1.0 %

Batch n° 138110

1-naphthylamine:	not detected
2-naphthol:	1201 ppm
1,6-dihydroxynaphthalene:	13 ppm
1,7-dihydroxynaphthalene:	120 ppm
Volatile content:	0.126%
Residue on ignition:	< 1%

3.1.6. Solubility

Solubility measured after 15 minutes sonication

Water:	0.019-0.029 % (w/v)
Ethanol:	50.2-75.3% (w/v)
DMSO:	27.1-40.7% (w/v)

3.1.7. Partition coefficient (Log P_{ow})

Log P_{ow}: 2.71 ± 0.19 (calculated)

3.1.8. Additional physical and chemical specifications

Melting point:	92 - 96 °C
Boiling point:	/
Flash point:	/
Vapour pressure:	/
Density:	/
Viscosity:	/
pKa:	/
Refractive index:	/
pH:	/
UV_Vis spectrum	/

3.1.9. Stability

PEG 400 solutions of 1-naphthol (0.05 and 200 mg/ml) were shown to be stable (within ± 3% of the initial value) for 24 hours when stored at room temperature and 7 days for the 0.05 mg/ml solution and 9 days for the 200mg/ml solution when stored at -20 ± 10 °C.

DMSO solutions of 1-naphthol (0.05 and 120 mg/ml) were shown to be stable (within ± 5% of the initial value) for 9 days when stored at -20 ± 10 °C.

Carboxymethylcellulose solution of 1-naphthol (2.0 and 100 mg/ml) were shown to be stable (within ± 8% of the initial value) for 10 days when stored at 2 - 8 °C.

The bulk test article (Batch n° 138110) was shown to be stable (100%), at room temperature and protected from light, during 10 weeks study period.

General Comments to physico-chemical characterisation

- Several batches of 1-naphthol, including unknown batches, have been used in various studies submitted for safety evaluation. However, complete chemical characterisation is provided for only batch n° 138110.
- Water solubility of 1-naphthol is not evaluated by EU Method A6.
- Log P_{ow}: calculated values cannot be accepted as estimates of the true physical constant without justification.
- The stability of 1-naphthol in marketed products is not reported.

3.2. Function and uses

1-Naphthol is used in oxidative hair dye formulations at a maximum concentration of 4.0%, which after mixing typically in 1:1 ratio with hydrogen peroxide prior to use, corresponds to a concentration of 2.0% upon application.

3.3. Toxicological Evaluation

3.3.1. Acute toxicity

3.3.1.1. Acute oral toxicity

Guideline:	/
Species/strain:	CFY rats, fasted
Group size:	5 per sex
Test substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	1000, 1600, 2500 and 4000 mg/kg bw
Route:	oral, suspension in 0.5% aqueous gum tragacanth + 0.5% Na_2SO_4
Exposure:	single administration and a 14 days observation period
GLP:	not in compliance
Date:	1975 (ref 2); 1977 (ref 3)

A dose finding study consisting of 2 animals per sex was performed. In a final study animals (5/sex) were exposed to 1-naphthol which was suspended in tragacanth gum containing 0.5% sodium sulphate. Animals were exposed to 40% suspension. Shortly after dosing the animals showed lethargy, piloerection, ptyalism and ataxia. Mortalities occurred from 2 to 67 hours post dosage and autopsy revealed darkening of the liver, kidneys and spleen.

The calculated LD50 was 2300 mg/kg bw (95% confidence limit from 1700 to 3300 mg/kg bw).

Ref.: 2, 3

Guideline:	/
Species/strain:	CD-1 mice, fasted
Group size:	2 per sex
Test substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	500, 1000 and 2000 mg/kg bw
Route:	oral, in propane-1,2-diol (1:1 v/v)
Exposure:	single administration and a 14 days observation period
GLP:	not in compliance
Date:	1988

Four mice (2/sex) were exposed to 1-naphthol at doses of 500, 1000 and 2000 mg/kg bw in propane-1,2-diol by gavage.
One male in the 500 mg/kg bw group was killed in extremis two hours post dosage. Other animals in this group showed piloerection and laboured respiration. Animals in the 1000 mg/kg bw group showed piloerection, but survived to the end of the study. Shortly after dosing animals exposed to 2000 mg/kg bw showed abnormal respiration and soon after dosing collapsed. All animals in this dosage group were killed in extremis from 15 to 90 minutes

The LD50 was estimated to be between 1000 to 2000 mg/kg bw.

Ref.: 4

3.3.1.2. Acute dermal toxicity

No data submitted

3.3.1.3. Acute inhalation toxicity

No data submitted

3.3.2 Irritation and corrosivity

3.3.2.1. Skin irritation

Guideline:	/
Species:	New Zealand white rabbits
Group:	3 (sex not stated)
Substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	2.5%
Vehicle:	water; in 0.5% aqueous gum tragacanth containing 0.05% sodium sulphite
GLP:	/
Date:	1977 (ref 3); 1975 (ref 6)

The skin irritation potential of 1-naphthol was evaluated in New Zealand White rabbits. Application of a 2.5% solution in aqueous gum tragacanth was made to the intact and abraded skin. The period of application was not stated. There was no reaction observed at 24 hours or 72 hours later.

Conclusion
Under the conditions of the experiment, a 2.5% aqueous suspension of 1-naphthol was considered not to be irritant to rabbit skin.

Ref.: 3, 6

3.3.2.2. Mucous membrane irritation

Guideline:	/
Species:	New Zealand white rabbits
Group:	3 (sex not stated) per test dose
Substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	0.5, 1.5, 2.0 and 2.5%
Vehicle:	water; in 0.5% aqueous gum tragacanth containing 0.05% sodium sulphite
GLP:	/
Date:	1977 (ref 3); 1975 (ref 5)

The eye irritation potential of 1-naphthol was evaluated in New Zealand White rabbits. Concentrations of 0.5, 1.5, 2 and 2.5% 1-naphthol were placed into one conjunctival sac. The eyes were rinsed with 50ml of water 10 seconds after instillation of the test material.

1-Naphthol caused corneal opacities, lasting for 1-3 days in 2/3 rabbits treated with 2% suspension, and in 1/3 rabbits treated with 2.5% suspension. A second rabbit treated with 2.5% showed "dulling of the normal corneal lustre" which lasted for 2 days. A rabbit with

corneal changes at 2.5% also had corneal swelling and a rabbit with corneal changes at 2% showed swelling and redness. One rabbit treated with 2.5% and a second with 2% showed mild conjunctival irritation. 2/3 rabbits treated with 1.5% and 1/3 treated with 0.5% also showed mild conjunctival irritation.

Conclusion
Although all effects were transient, all tested aqueous suspension of 1-naphthol showed irritant effects with an increasing degree of eye irritation with increasing dose.

Ref.: 3, 5

3.3.3. Skin sensitisation

Local Lymph Node Assay (LLNA)

Guideline:	OECD 429
Species:	CBA/J mice
Group:	18 females; 3 for each of 5 test groups (with 3 controls)
Substance:	1-naphthol
Batch:	Lot I 6694
Purity:	> 99%
Dose:	1-naphthol 0.1, 0.25, 0.5, 1 and 2.5% in 4:1 acetone:olive oil vehicle; 12.5 µl applied on days 1, 2 and 3
Vehicle:	4:1 acetone:olive oil
Control:	alpha hexylcinnamaldehyde (5, 10 and 25% in same vehicle)
GLP:	in compliance
Date:	3 July – 8 August 2001

12.5 µl 1-naphthol 0.1, 0.25, 0.5, 1 and 2.5% in 4:1 acetone:olive oil was applied on days 1, 2 and 3 by topical application to the ventral and dorsal surfaces of each ear. Five days after the first topical application, the mice were injected intravenously with ^{3}H-methyl thymidine, five hours later killed and the draining lymph nodes excised and pooled. Single cell suspensions were prepared and the proliferation capacity determined.

Mean stimulation indices are tabulated below:

Concentration (% w/v)	Stimulation Index
0.1	1.4
0.25	1.0
0.5	1.2
1.0	1.5
2.5	8.5

(The SI for the positive control was 2.4, 3.7, and 7.0 respectively for the 5, 10 and 25% dilutions).

1-Naphthol produced evidence of allergic contact sensitisation in this study at when tested at 2.5%. The EC3 value was calculated to be 1.3.

Ref.: 9

Comment
With an EC3 value of 1.3, 1-naphthol is a 'strong' sensitizer.

Guinea pig studies

Guideline:	/
Species:	Pirbright white guinea pigs
Group:	20 (but only 19 reported)
Substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	3% dilution
Vehicle:	mixture of Natrasol (2%), Tween 80 (2%), Sodium sulphite (0.05%), water (82.9%) and isopropanol (10%)
Control:	vehicle
GLP:	/
Date:	1976

An open epicutaneous test involved the application of a 3% dilution of 1-naphthol in the vehicle described above, to a 6cm^2 area of shaved flank skin for 6/7 days each week for 3 weeks. Following a 2 week rest period, there was a single application of the substance to the contra-lateral flank.

No reaction was observed in any of the 19 animals reported.

During the same experimental period, the laboratory was also testing other hair dye chemicals, including p-phenylenediamine, 2,5–diaminotoluene sulphate, 4-nitro-1,2-phenylenediamine to which 17 – 18 /20 animals showed an allergic elicitation response.

Ref.: 8

Guideline:	/
Species:	guinea pigs
Group:	20 with an additional 8 tested only at the challenge phase
Substance:	1-naphthol
Batch:	/
Purity:	/
Dose:	0.1% dilution in water (induction) for injection and topical application. Challenge with 0.1 and 0.05% in water
Vehicle:	water
Control:	vehicle
GLP:	/
Date:	1978

Three pairs of simultaneous injections were made on either side of a 4x6cm clipped area over the shoulder of each animal. A row of 3 injections were made on each side with a) 0.1ml Freund's complete Adjuvant, b) 0.1ml of test substance, and c) 0.05ml test substance emulsified with 0.05ml Adjuvant. One week after injection, the same area was clipped and covered with a 4x2cm patch saturated with the test substance and occluded for 48 hours. The animals were challenged after 2 weeks.

No reaction was observed on the skin of any animal following challenge with either 0.05 or 0.1% 1-naphthol.

Ref.: 7

Comment
The concentration of 1-naphthol used in the 2 Guinea pig studies does not conform to the guidelines (too low).

3.3.4. Dermal / percutaneous absorption

Guideline:	OECD 428
Tissue:	human skin; dermatomed thickness 400µm
Group size:	12 intact membranes per experiment (8 donors)
Diffusion cells:	exposed membrane area 2.54cm^2.
Skin integrity:	electrical resistance. Membranes ≤10 kΩ excluded
Test substance:	1-naphthol
Batch:	I-38110
Purity:	99.9% (w/w)
Labelled Test substance:	[^{14}C]-1-naphthol
Labelled Batch:	020K9440/41 (N9517-14C: analytical certificate)
Labelled Purity:	96.9% (certificate of analysis)
Test item:	4% 1-naphthol in 'blank' formulation (Nice'n Easy™ tint) a) with peroxide developer to give 2% 1-naphthol b) with placebo developer to give 2% 1-naphthol
Doses:	20 mg of test formulation/cm^2 skin (400 µg 1-naphthol /cm^2 skin)
Receptor fluid:	4% polyoxyethylene-20-oleyl ether solution in PBS
Solubility receptor fluid:	> 0.3 mg/ml w/v
Stability:	/
Method of Analysis:	liquid scintillation counting (limit 0.004µg/ml)
GLP:	in compliance
Date:	16 – 29 September 2004

The percutaneous absorption of 1-naphthol from a proprietary oxidative hair dye base containing 4% 1-naphthol was evaluated in an *in vitro* assay using human dermatomed skin. Prior to dosing, the formulation was mixed 1:1 with either A) a hydrogen peroxide developer solution to give a final concentration of 2% 1-naphthol or B) a placebo developer to give a final concentration of 2% 1-naphthol.
A dose of 20 mg of test formulation/cm^2 skin (400 µg 1-naphthol /cm^2 skin) was applied to the skin samples for 30 minutes followed by thorough rinsing with 3% Teepol®. Measurements of the 1-naphthol penetrating the skin into the receptor fluid were taken following the 30 minute exposure period and at set intervals during the 48 hour measurement period (1, 2, 4, 6, 24, 29 and 48 hours post application). At the end of the 48 hour measurement period, tape stripping was conducted and the levels of 1-naphthol in the tape strips and the remaining epidermis/dermis determined.

Results

a) In the oxidative formulation the amount considered absorbed was 3.58 ± 1.13 (range 1.31 to 5.46 µg/cm².
b) In the placebo, non-oxidative formulation the amount considered absorbed was 3.60 ± 1.80 (range 1.49 to 8.28) µg/cm² [0.899 ± 0.451 (range 0.373 to 2.07) % of the applied dose].

Conclusion

In the oxidative formulation the amount considered absorbed was 3.58 ± 1.13 (range 1.31 to 5.46) µg/cm² [0.894 ± 0.283 (range 0.747 to 1.37) % of the applied dose].

Ref.: 10

Comment

An A_{max} of 5.46 µg/cm² can be used for calculating the MOS as too few test chambers were used.

3.3.5. Repeated dose toxicity

3.3.5.1. Repeated Dose (28 days) oral / dermal / inhalation toxicity

Guideline:
Species/strain: CD-1 mice
Group size: 5 per sex and per dose
Test substance: 1-Naphthol
Batch: /
Purity: /
Dose: 0, 50, 100, 200 mg/kg bw/day
Route: oral
Vehicle: propane-1,2-diol - water, 1:1 v/v
Exposure: by oral gavage
GLP: not in compliance
Date: 1988

The mice were dosed by oral gavage for 30 days with 0, 50, 100, 200 mg/kg bw/day doses of 1-naphthol in propane-1,2-diol. Two negative control groups were used, one being untreated and the other being dosed with the vehicle. All animals were killed either at the end of the study or *in extremis*. The blood samples were taken for clinical chemistry and haematology analysis, a full post mortem examination was subjected. Samples were taken from colon, duodenum, gall bladder, heart, stomach and thyroid gland.

Results
Treatment related changes were seen in glandular stomach as focal mucosal erosion in three male mice dosed at 200 mg/kg bw/day. Two of these animals were killed in extremis on the fourth and twentieth days of the study. The third animal which survived to the end of exposure also showed focal erosion of the glandular stomach. No gastric effects were seen in the female mice dosed at 200 mg/kg bw/day or in the other treatment groups. Exposure was accompanied by increase in white blood cell counts, the response being dose related in the female mice. However, the increases were all within historical normal limits of the laboratory. The weight gain was affected by the treatment, however the effect was not dose related.

Conclusions
The gastric lesions showed a sex difference, with the male mice having a NOAEL of 100 mg/kg bw/day. NOAEL for female mice was higher than the highest dose applied (200 mg/kg bw/day).

Ref.: 4

3.3.5.2. Sub-chronic (90 days) oral / dermal / inhalation toxicity

Guideline: OECD 408 (1981)
Species/strain: Crl:CD/(SD)BR VAF/Plus rats;
Group size: 15 per sex and per dose
Test substance: RE1141.03
Batch: Lot n° 03
Purity: 99.7%
Dose: 0, 65, 130, 400 mg/kg bw/day
Route: oral, in carboxymethylcellulose 0.5%
Exposure: by oral gavage
GLP: in compliance
Date: 20 April – 22 July 1998

The dosages were based on a dose finding study (2 weeks)

Male and female Crl:CD/(SD)BR VAF/Plus rats were assigned to eight groups (15 animals/sex/group in control and exposure groups/90 days and five animals/sex/group in control and exposure groups/ 7 days). Each group was dosed to 65, 130, or 400 mg/kg bw/day or vehicle only. Food and water was provided *ad libitum.* The animals were observed twice daily for mortality/morbidity. Body weights were recorded for each animal and food consumption data were collected weekly. Ophthalmic examinations were done before initiation of exposure and during the week 13 for animals exposed 90 days. On day 7 (animals in groups 5 through 8) and once during weeks 4 and 14 (animals in groups 1 through 4), blood and urine samples were collected for haematology, clinical chemistry and urine chemistry tests. On day 7, animals in groups 5 through 8 were sacrificed and during week 14, animals in groups 1 through 4 were anesthetized, weighed, exsanguinated, and necropsied. Microscopic examinations were done on tissues from each animal in the control and 400 mg/kg bw/day exposed group, respectively. The lungs, liver, kidneys, stomach, spleen, and macroscopic lesions were examined microscopically from each animal given 65 or 130 mg/kg bw/day. Sperm collected from each male was evaluated for motility, morphology, and concentration.

Results
No mortality occurred during the study. Discoloured fur (brown perineal or general yellow hair coat) was noted in females given 400 mg/kg bw/day. Food consumption for males and females was similar in exposed and control groups. No differences in body weight or body weight gain or differences in ophthalmic observations were reported. The sperm motility, morphology, and count were not affected. A number of urine and clinical chemistry parameters were altered, however none of these findings were considered adverse. Microscopically, treatment-related changes were restricted to the stomach and spleen of animals given higher doses of the test material. In gastric tissues, squamous hyperplasia and hyperkeratosis of the nonglandular stomach were present in all males and most females given 400 mg/kg bw/day; and in both sexes at130 mg/kg bw/day. At the high-dose level, gastric changes were moderate to severe and in both sexes given 130 mg/kg bw/day were minimal to mild. In the spleen sections, increased pigment deposits (hemosiderin) were minimally to slightly increased in the 400 mg/kg bw/day group. Treatment-related stomach or changes in spleen were not observed in rats at the 65 mg/kg bw/day group.

Conclusion
The study authors set the NOAEL for RE1141.03 at 130 mg/kg bw/day, based on the microscopical changes in stomach and in spleen. In the submission, however, a value of 65 mg/kg bw/day was mentioned.

Ref.: 12

Comment
The SCCP agrees with the study authors to set the NOAEL at 130 mg/kg bw.
In contrast to the teratogenicity study (ref 19), lacrimation was not reported in the 90-days study.

3.3.5.3. Chronic (> 12 months) toxicity

No data submitted

3.3.6. Mutagenicity / Genotoxicity

3.3.6.1 Mutagenicity / Genotoxicity *in vitro*

Bacterial Reverse Mutation Test

Guideline:	OECD 471
Species/strain:	TA 98, TA 100, TA 1535, TA 1537, WP2*uvrA* (pKM101)
Replicates:	2 replicates in the initial test and three replicates in the confirmatory test
Test substance:	GTS03979
Solvent:	DMSO
Batch:	I-38110
Purity:	99.9%
Concentrations:	initial test: 2.5, 5, 20, 50, 200, 500, 2000, 5000 μg/plate confirmatory test: 10, 25, 50, 100, 200, 500 μg/plate
Treatment:	Pre-incubation test was applied, both with and without Aroclor induced metabolic activation
GLP:	In compliance
Date:	9 August 2004 – 16 August 2005

Results
In the initial test, signs of toxicity were observed at ≥ 500 μg/plate in the presence of metabolic activation and at ≥ 200 μg/plate in the absence of metabolic activation. Except TA 98 with metabolic activation, there were no indications of an increase in the mutant frequency at any concentration in the tester strains either with or without metabolic activation. In TA 98 with metabolic activation, a clear concentration related increase in the mutant frequency until 50 μg/plate was observed with a 7-fold increase. A review of the raw data indicated that the dosing of tester strains TA 98 and TA 100 in the presence of metabolic activation was repeated in the initial test due to a technical problem with the initial dosing. This repeat dosing occurred two hours after the original dosing. In the confirmatory test, the dosing took place as soon as possible following dose formulation. In the confirmatory test there were no indications of an increase in the mutant frequency at any concentration in the tester strains either with or without metabolic activation. Thus, the increase in mutant frequency with TA98 in the presence of metabolic activation was not reproduced. In order to investigate if the two-hour delay in using the dose formulations had any impact on the response observed with TA98 in the initial test, a repeat assay was performed with TA98 in the presence of S9 mix. In this repeat assay two dose formulations were prepared and one was dosed immediately after preparation and one was dosed two hours after preparation. This repeat assay showed no indications of an increase in the mutant frequency at any concentration and there was no difference in the results obtained with the formulations used immediately after preparation or used two hours after preparation.

Conclusion
Under the test conditions used GTS03979 did not induce gene mutations in bacteria.

Ref.: 13

***In vitro* Mammalian Cell Gene Mutation Test (*tk*$^{+/-}$ locus)**

Guideline:	OECD 476
Species/strain:	Mouse lymphoma cell line L5178Y
Replicates:	Single culture in one experiment
Test substance:	GTS03979

Solvent:	DMSO
Batch:	I-38110
Purity:	99.9%
Concentrations:	With metabolic activation: 0.4, 0.6, 0.8, 1, 1.2, 1.3, 1.4, 1.6 μg/ml Without metabolic activation: 10, 20, 40, 50, 60, 70, 80 and 90 μg/ml
Treatment	With and without Aroclor induced metabolic activation: 4-hour treatment and 48 h expression period
GLP:	In compliance
Date:	8 September 2004 – 4 August 2005

The test substance was examined for its mutagenic activity in the L5178Y $tk^{+/-}$ mouse lymphoma test in the absence and presence of metabolic activation. A preliminary toxicity test was conducted. In the presence of metabolic activation ten concentrations were tested ranging from 0.0313 to 4 μg/ml and in the absence of metabolic activation 10 concentrations ranging from 2.35 to 1200 μg/ml. As positive controls MMS (methyl methanesulfonate) for testing without metabolic activation and MCA (methylcholanthrene) for testing with metabolic activation were used.

Results
In the preliminary toxicity test, severe toxicity was observed > 2 μg/ml in the presence of metabolic activation and > 75 μg/ml in the absence of metabolic activation. Based on these data the main experiment was performed between 0.4 to 1.60 μg/ml in the presence of metabolic activation. In the absence of metabolic activation, 10 to 90 μg/ml were tested. In the presence of metabolic activation, toxicity ranged from no cytotoxicity to high cytotoxicity (100% to 16% relative total growth). A concentration related increase was observed in the mutant frequency. However, it was weak and the highest induction of mutant frequency was observed at the highest concentration (1.6 μg/ml) tested with a mutant frequency of 32 x 10^{-6} greater than the control. This increase was much less than the required 90 induced mutants per 10^6 clonable cells above the control value for obtaining a positive response. In the absence of metabolic activation toxicity levels ranged from 94% relative total growth to 11% at the highest concentration. A clear concentration related increase in mutant frequency was observed. Treatments of 60, 70, and 90 μg/ml induced a mutant frequency that met the criteria for a positive response. Mutant colonies from the positive controls MMS (methyl methanesulfonate for testing without metabolic activation) and MCA (methylcholanthrene for testing with metabolic activation) treated cultures showed both small and large colonies. The test article doses (60, 70 and 90 μg/ml without metabolic activation) which exhibited a positive response, showed a preferential increase in small colonies indicating larger mutations.

Conclusion
Under the test conditions used GTS03979 is considered mutagenic in the absence of metabolic activation.

Ref.: 15

Comment
Four mutation assays in the presence of metabolic activation were initiated, but the first trial was unacceptable due to excessive cytotoxicity. The second mutation assay in the presence of metabolic activation was terminated due to a technical error during dosing. The third mutation assay in the presence of metabolic activation was also terminated due to excessive cytotoxicity. The fourth mutation assay was considered acceptable. The increase in small colonies may indicate clastogenicity.

In vitro chromosome aberration test

Guideline:	OECD 473
Species/strain:	Chinese hamster ovary cells (CHO-WBL)

Replicates:	duplicate cultures in 1 experiment
Test substance:	GTS03979
Solvent:	DMSO
Batch:	I38110
Purity:	99.9%
Concentrations:	Initial toxicity assay: 1.2, 4, 12, 40, 120, 400 and 1200 μg/ml Main assay: 4 h treatment, with and without S9-mix: 30, 60 and 90 μg/ml 20 h treatment, without S9-mix: 5, 10, and 20 μg/ml
Treatment:	Initial toxicity assay and Main assay with Aroclor induced metabolic activation: 4 hours treatment and harvest time 20 h after start of treatment. Without metabolic activation: 4 and 20 hours treatment and harvest time 20 h after start of treatment
GLP:	In compliance
Date:	9 August 2004 – 4 August 2005

Results
In the initial toxicity assay (4-hour treatment without metabolic activation), no cell growth ≥ 400 μg/ml and precipitation was visible. The reduction in cell growth at 120 μg/ml was 57%. In the presence of metabolic activation, precipitation was visible at 1200 μg/ml. The reduction in cell growth was 72% at 12 μg/ml. In the assay without metabolic activation with 20-hour treatment, precipitation was visible after dosing at 1200 μg/ml. At 120 μg/ml the reduction in cell growth was 99%.
Based on the results of the initial toxicity assay, the main assay was conducted using 11 concentrations between 7.5 and 400 μg/ml for 4-hours treatment without metabolic activation. Chromosomal aberrations were analysed from the cultures treated with 30, 60 and 90 μg/ml, giving reductions in cell growth of 28%, 38% and 50% respectively. A statistically significant increase in cells with polyploidy was observed in the cultures treated with 60 μg/ml. Moreover, a statistically significant increase in cells with endoreduplication at all three concentrations was observed in a concentration-related manner. Finally, a concentration-related increase in cells with chromosomal aberrations was observed and the increase was statistically significant at 90 μg/ml.
In the assay without metabolic activation with 20-hours treatment, precipitation was not observed. The assay was conducted using 12 concentrations between 1.25 and 120 μg/ml. Chromosomal aberrations were analysed from the cultures treated with 5, 10 and 20 μg/ml, giving reductions in cell growth of 9%, 17% and 55% respectively. A statistically significant increase was observed in cells with polyploidy in the cultures treated with 10 μg/ml. There were no indications of increases at any concentration in cells with chromosomal aberrations or endoreduplication.

In the assay with metabolic activation with 4-hours treatment precipitation was not visible. The assay was conducted using 11 concentrations between 0.5 and 4 μg/ml. Chromosomal aberrations were analysed from the cultures treated with 1, 2 and 2.5 μg/ml, giving a reduction in cell growth of 54% at the highest concentration. There was a concentration-related increase in cells with chromosomal aberrations and the increase was statistically significant at 2.5 μg/ml. There were no indications of increases at any concentration in cells with endoreduplication or polyploidy.

Conclusion
Under the test conditions used the test article GTS03979 induced structural aberrations with and without metabolic activation. There was also an indication that the test article has an aneugenic potential and may inhibit cell cycle progression.

Ref.: 14

3.3.6.2 Mutagenicity/Genotoxicity *in vivo*

Mammalian Erythrocyte Micronucleus Test

Guideline:	OECD 474
Species/strain:	Mice, CD-1®(ICR)BR
Group size:	5 males per dose group and per sacrifice time
Test substance:	GTS03979
Batch:	I-38110
Purity:	99.9%
Dose level:	125, 250 and 500 mg/bw administered as single dose
Route:	Oral gavage
Vehicle:	Polyethylene glycol 400 (PEG 400)
Sacrifice times:	24 and 48 hours (high dose only)
GLP:	In compliance
Date:	2 September 2004 – 4 August 2005

A dose range-finding study was conducted and the test article was formulated in PEG 400 and administered once by oral gavage to three males and three females per dose level. The animals were dosed at 500, 1000, or 2000 mg/kg bw and observed for up to 2 days after dosing for toxic signs and/or mortality. Mortality was observed in 1/3 males in the 500 mg/kg bw dose group, 1/3 males and 1/3 females in the 1000 mg/kg bw dose group, and in 1/3 males and 1/3 females in the 2000 mg/kg bw. Clinical signs of toxicity observed in these animals prior to being found dead included slight hypoactivity, ataxia, and/or irregular respiration. Based on the results of the dose range-finding assay, GTS03979 was administered once in PEG 400 at three doses, the highest dose being 500 mg/kg bw (estimated maximum tolerated dose) to groups of five male mice per bone marrow sampling time. An additional group of six male mice were dosed at 500 mg/kg bw for use as possible replacements in the event of mortality. Five animals from all the groups were sacrificed 24 hours after dosing and from the vehicle control and high dose group at 48 hours after dosing. Plasma samples were collected at 1, 2, 4, 6, 8, 24 and 48 hours after dosing for detection of the test article (satellite group). For all groups at 24 hours and vehicle and high dose group only at 48 hours, bone marrow was extracted and at least 2000 PCEs per animal were subsequently microscopically analyzed for the frequency of micronuclei. Cytotoxicity was assessed by scoring the number of PCEs and normochromatic erythrocytes (NCEs) in at least the first 1000 total erythrocytes for each animal. Cyclophosphamide (CP) was used as positive control.

Results
There were no signs of clinical toxicity in the animals treated at concentration levels up to 500 mg/kg bw. There were no indications of an increase in micronucleated PCEs at any concentration tested, 24 or 48 hours after the mice were sacrificed. There were no signs of cytotoxicity, expressed as a decreased PCE:NCE ratio observed in any dose group. However bioanalytical evaluation of plasma samples collected from high dose group animals showed the presence of test material and thus confirmed target organ exposure. The peak mean plasma concentration (~648 ng/ml) was observed at approximately 1 hour after test material administration.

Conclusion
Under the test conditions used, GTS03979 is not considered clastogenic in the bone marrow micronucleus test in mice.

Ref.: 16

In vivo Unscheduled DNA Synthesis (UDS) Test in Rats

Guideline:	OECD 486
Species/strain:	Rats, Crl:CD®(SD)IGS BR
Group size:	Control and low dose group: 3 males per dose group and per sacrifice time High dose group: 5 males per sacrifice time
Test substance:	GTS03979
Lot no:	I-38110
Purity:	99.9%
Dose level:	875 and 1750 mg/bw administered as single dose
Route:	Oral gavage
Vehicle:	Polyethylene glycol 400 (PEG 400)
Sacrifice times:	2-4 and 12-16.4 hours
GLP:	In compliance
Date:	23 December 2004 – 4 August 2005

In a dose range-finding study, three male and three female rats per dose level were dosed once by oral gavage. The animals were dosed at 1500 or 2000 mg/kg bw and observed for up to 2 days after dosing for toxic signs and/or mortality. Clinical signs included salivation, irregular respiration, hypoactivity, piloerection, hunched posture, red nasal/oral crust, non-formed faeces and/or brown anal-genital stain. One female dosed at 2000 mg/kg bw was found dead one day after dosing. Based on the results of the dose range-finding assay, the test article was administered once in PEG 400 at doses of 875 and 1750 mg/kg bw to groups of three male rats per time-point in the low dose group. Five animals per time-point were treated in the high dose group. All animals from each group were perfused for the collection of hepatocytes and establishment of cultures. With the exception of the positive control at the 12-16 hour time point, cultures from three animals per group were evaluated for UDS (two were evaluated for the 12-16 hour positive control). For the early UDS time point, perfusions were initiated 2.6 to 3.0 hours after dose administration. For the 12- to 16-hour time point, perfusions were initiated 15.9 to 16.4 hours after dose administration. Dimethylnitrosamine was used as positive control.

Results
For the 2-4 hours UDS time-point, the hepatocytes ranged in viability (determined by trypan blue dye exclusion) from 52.7 to 86.4% of the total cells collected in the perfusate. The attachment efficiency varied from 18.7 to 103.1%, and the viability of the attached cells was good, ranging from 89.9% to 99.7%. For the 12- to 16-hour time-point, the hepatocytes ranged in viability from 29.9% to 93.5% of the total cells collected in the perfusate. The attachment efficiency varied from 0.4% to 152.1%, and the viability of the attached cells ranged from 8.3% to 100.0%.

For the 2- to 4-hour time point, there were no indications of an increase in the mean net nuclear grain count compared to the control at both dose levels. For the 12- to 16-hour time-point, there were no indications of an increase in the mean net nuclear grain count compared to the control at both dose levels. There were no difference between the control values and the two doses tested in the percentage of cells in repair (cells with $\geq$ 5 net nuclear grains) for both the 2- to 4-hour and 12- to 16-hour time-point.

Conclusion
Under the test conditions used GTS03979 is not considered genotoxic in the *in vivo* unscheduled DNA synthesis test.

Ref.: 17

3.3.7. Carcinogenicity

Guideline:	/
Species/strain:	Male and female weanling Sprague Dawley rats
Group size:	60 animals per sex
Test substance:	hair dye formulations n° 7403 containing 0.5% 1-naphthol prior to mixing with an equal volume of 6% hydrogen peroxide.
Batch:	/
Purity:	/
Dose:	0.5 ml of the test formulation
Route:	Topical application twice weekly
Exposure:	114 weeks
GLP:	not in compliance
Date:	1987

The experiment involved 12 treatment groups (9 oxidative and 3 non-oxidative hair dye formulations) and 3 negative control groups.

60 male and 60 female were obtained from the first F1a-litter of a multi-generation reproduction study in rats treated with the same hair dye formulation (4703) containing 0.5% 1-naphthol. The F0 parents had received topical application of the hair dye formulation from the time of their weaning to the weaning of their offspring. The dye formulation was administered topically to the shaved (24 hours prior to application) neck and back area twice weekly. The initial dosage level of 0.2 ml/rat was increased incrementally by 0.1 ml per week until 0.5 ml was achieved. There were three independent control groups each containing 60 males and 60 females, which received no treatment.
The rats were observed daily for overt signs of toxicity and for mortality. Detailed observations were recorded weekly. Individual body weights were recorded weekly for the first 14 weeks and monthly thereafter. Group food consumption was recorded weekly. Haematological, biochemical and urinalysis studies were done on 5 males and 5 females per group at 3, 12, 18 and 24 months. After 12 months of treatment, 5 males and 5 females from each group were sacrificed and necropsied. Histopathological evaluations were performed on 18 tissues (plus tumour masses) including treated skin.

Results
Prior to terminal sacrifice (at week 114), the survival was 22 males and 14 females for the exposed group. Survival was 17 – 20 males and 22 – 26 females for the control groups.
There were no significant changes in haematological values in the treated groups at 18 and 24 months. No significant differences considered to be treatment related were observed in the biochemical studies or in the urinalysis. Non-neoplastic lesions were those commonly found in ageing rats and were considered to be spontaneous.
The incidence of pituitary adenomas in males and females was slightly higher than in all three control groups, but the high background incidence (in total 6 formulations containing different hair dyes were tested) of this lesion casts doubt on the biological significance of this finding.

Conclusion
It was concluded that no increased tumour incidence were found in any of the tissues examined.

Ref.: 21

Comment
2,4-Diaminoanisole (EU, carcinogenic. Cat. 2) was tested in the same experiment and no response was found. It should also be noted that the concentration of 1-naphthol was only 0.5%.

Taken from opinion SCCNFP/0130/99

One oxidative formulation (7403, mixed 1:1 with 6% hydrogen peroxide) containing 0.5% 1-naphthol was tested on Swiss Webster mice by dermal application (0.05 ml/cm² for 21 months). No adverse effects were reported.

Ref.: 22

Comment
The experiment involved 12 treatment groups (9 oxidative and 3 non-oxidative hair dye formulations) and 3 negative control groups. 2,4-Diaminoanisole (EU, carcinogenic. Cat. 2) was tested in the same experiment and no response was found. It should also be noted that the concentration of 1-naphthol was only 0.5%.

General comment
No conclusion with regard to carcinogenicity can be made from the studies.

3.3.8. Reproductive toxicity

3.3.8.1. Two generation reproduction toxicity

A multi-generation reproduction toxicity study was carried out by using a formulation #7403 containing 0.5% 1-Naphthol Because of the poor study design (poor test substance, details of negative control group is not stated and a viral infection resulted in poor reproductive performance in all groups) the study it was considered to be of limited value only.

Ref.: 21

3.3.8.2. Teratogenicity

Guideline:	OECD 414
Species/strain:	CRL:CD(SD)BR VAF/Plus (Sprague-Dawley)
Group size:	100 female (25/group)
Test substance:	RE-1141.02
Batch:	02
Purity:	99.7%
Dose:	0, 20, 100, 400 mg/kg bw/day
Vehicle:	aqueous 0.5% carboxymethylcellulose
Route:	oral
Exposure:	by oral gavage, 10 ml/kg bw
GLP:	in compliance
Date:	20 January 1998 – 12 February 1998

A dose finding study at dose levels of 20, 120, 600 and 1000 mg/kg bw/day preceded this study.

Twenty-five pregnant female rats were assigned to each of four dosage groups. The test substance or aqueous 0.5% carboxymethylcellulose (control) was administered via gavage once daily on days 7 through 17 of presumed gestation. Vehicle and dosages of 20, 100, and 400 mg/kg bw/day were administered daily. Animals were observed for viability at least twice each day of the study. Body weights were recorded daily during the dosage and post-dosage periods and feed consumption values were recorded. All rats were sacrificed by carbon dioxide asphyxiation on day 20, and a gross necropsy of the thoracic, abdominal and pelvic viscera was performed. The number of corpora lutea in each ovary was recorded. The uterus of each rat was examined for pregnancy, number and distribution of implantations, live and dead foetuses and early and late resorptions. Each foetus was identified, weighed

and examined for sex and gross external alterations. Approximately one-half of the foetuses in each litter were examined for soft tissue alterations and the remaining foetuses in each litter examined for skeletal alterations.

Results
No deaths, abortions or premature deliveries occurred during this study. Statistically significant numbers of rats in the 400 mg/kg bw/day dosage group had excess salivation, dilated pupils, decreased motor activity, ataxia, impaired righting reflex, lacrimation, lost righting reflex, lethargy, red, brown or orange perioral substance, urine stained abdominal fur, rales, chromorhinorrhea, twitches, body jerks and brown perinasal substance. Additionally, dilated pupils, lacrimation, brown perioral substance and chromorhinorrhea occurred in one to five rats in the 100 mg/kg bw/day dosage group; the incidence of chromorhinorrhea was statistically significant. No gross lesions were identified at necropsy that was considered treatment related. Body weight gains and absolute and relative feed consumption values were significantly reduced for the entire dosage period in the 400 mg/kg bw/day group. Maternal body weights were significantly reduced compared to the control group. Average foetal body weights were reduced by 4% as compared to controls in the 400 mg/kg bw/day dosage group; these reductions were significant for total and female foetal body weights. No other Caesarean-sectioning or litter parameters were affected by exposure to the test substance to the dams at dosages as high as 400 mg/kg bw/day. (No typical changes in skeletal ossification those are indicative of developmental delay and which would have been expected to accompany significant foetal weight decrements).
The slight foetal body weight reduction might be influenced by maternal toxicity.

Conclusion
The maternal NOEL of RE-1141.02 was 20 mg/kg bw/day because of a significant incidence of chromorhinorrhea, dilated pupils and lacrimation of some animals in the 100 mg/kg bw/day group. The developmental NOAEL was set at 400 mg/kg bw/day, the highest dose applied.

Ref.: 19

3.3.9. Toxicokinetics

No data submitted

3.3.10. Photo-induced toxicity

3.3.10.1. Phototoxicity / photoirritation and photosensitisation

No data submitted

3.3.10.2. Phototoxicity / photomutagenicity / photoclastogenicity

No data submitted

3.3.11. Human data

No data submitted

3.3.12. Special investigations

No data submitted

3.3.13. Safety evaluation (including calculation of the MoS)

CALCULATION OF THE MARGIN OF SAFETY

(1-Naphthol)
(oxidative - permanent)

Maximum absorption through the skin	**A (µg/cm^2)**	**=**	**5.46 µg/cm²**
Skin Area surface	**SAS (cm^2)**	**=**	**700 cm^2**
Dermal absorption per treatment	**SAS x A x 0.001**	**=**	**3.82 mg**
Typical body weight of human		**=**	**60 kg**
Systemic exposure dose (SED)	**SAS x A x 0.001/60**	**=**	**0.064 mg/kg bw**
No observed effect level (mg/kg bw) (maternal toxicity, oral, rat)	**NOEL**	**=**	**20 mg/kg bw**
Margin of Safety	**NOEL / SED**	**=**	**312**

3.3.14. Discussion

Physico-chemical properties
1-Naphthol is used in oxidative hair dye formulations at a maximum concentration of 4.0%, which after mixing typically in 1:1 ratio with hydrogen peroxide prior to use, corresponds to a concentration of 2.0% upon application.
Several batches of 1-naphthol, including unknowns, have been used in various studies submitted for the safety evaluation. However, complete chemical characterisation is provided for only batch no. 138110.
Water solubility of 1-naphthol is not evaluated by EU Method A6. Log P_{ow} is not experimentally determined and stability of 1-naphthol in marketed products is not reported.

General toxicity
The LD50 was estimated to be between 1000 to 2000 mg/kg bw.
The repeated daily oral administration of 1-naphthol to rats for 13 weeks at 65, 130, or 400 mg/kg bw/day resulted in a number of altered urine and clinical chemistry parameters. However none of these findings were considered adverse. Microscopic, treatment-related changes were restricted to the stomach and spleen. In gastric tissues, squamous hyperplasia and hyperkeratosis of the nonglandular stomach were present in all males and most females given 400 mg/kg bw/day; and in both sexes at 130 mg/kg bw/day. At the high-dose level, gastric changes were moderate to severe and in both sexes given 130 mg/kg bw/day were minimal to mild. Treatment-related stomach or changes in spleen were not observed in rats at the 65 mg/kg bw/day group. The NOAEL was set at 130 mg/kg bw.
The maternal NOEL of the test substance RE-1141.02 was 20 mg/kg bw/day because of a significant incidence of chromorhinorrhea, dilated pupils and lacrimation of some animals in the 100 mg/kg bw/day group. The developmental NOAEL was set at 400 mg/kg bw/day, the highest dose applied.

Irritation / sensitisation
A 2.5% aqueous suspension of 1-naphthol was considered not to be irritant to rabbit skin. Although all effects were transient, aqueous dilutions of 1-naphthol of 0.5 to 2.5% caused eye irritation to rabbits with irritant effects increasing with increasing dose.
With an EC3 value of 1.3, 1-naphthol is a 'strong' sensitizer.

Dermal absorption
In an oxidative formulation containing 2% 1-naphthol, the amount considered absorbed was 3.58 ± 1.13 (range 1.31 to 5.46) μg/cm^2 [0.894 ± 0.283 (range 0.747 to 1.37) % of the applied dose]. In the experiment, 12 dermatomed human skin samples were used (8 donors). The A_{max} of 5.46 μg/cm² can be used for calculating the MOS.

Mutagenicity / genotoxicity
1-Naphthol has been sufficiently investigated for the three types of mutations: gene mutation, structural and numerical chromosomal aberrations. 1-Naphthol did not induce gene mutations in bacteria. 1-Naphthol induced clastogenic effects in Chinese hamster ovary cells and gene mutations in the mouse lymphoma assay with mammalian cells (L5178Y) in the absence of metabolic activation. The increase in small colonies may indicate clastogenicity. The genotoxic/clastogenic effects observed in the *in vitro* assays could not be confirmed in two *in vivo* assays. There were no signs of genotoxic effects of 1-naphthol tested *in vivo,* based on micronucleus test of bone marrow in mice and the unscheduled DNA synthesis (UDS) test in rats.
1-Naphthol, itself, is not considered to have *in vivo* genotoxic potential. However, appropriate tests with 1-naphthol in combination with hydrogen peroxide should be provided.

Carcinogenicity
A non-oxidative hair dye formulation containing 0.5% 1-naphthol together with 12 other dye ingredients has been tested for carcinogenicity in mice and rats by topical application. No increase in tumour frequency was found. No conclusion with regard to carcinogenicity can, however, be made from the studies due to the low concentration of 1-naphthol used and the fact that the experimental procedure used did not give any response when 2,4-diaminoanisole (EU, carcinogenic Category 2) was tested.

4. CONCLUSION

The SCCP is of the opinion that, apart from the risks associated with the use of a strong sensitiser, the use of 1-naphthol itself in oxidative hair dye formulations at a maximum concentration of 2.0% on the head, does not pose any other risk to the health of the consumer.

1-Naphthol itself has no mutagenic potential. However, studies on genotoxicity/mutagenicity in finished hair dye formulations should be undertaken following the relevant SCCNFP/SCCP opinions and in accordance with its Notes of Guidance.

5. MINORITY OPINION

Not applicable

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