



EUROPEAN COMMISSION



Scientific Committee on Consumer Products

SCCP

OPINION ON HC Red n° 10 + HC Red n° 11

COLIPA n° B71



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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http://ec.europa.eu/health/ph_risk/risk_en.htm

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1. BACKGROUND

Submission I for HC Red n° 10 + HC Red n° 11 with the chemical names for HC Red n° 10: 1-Amino-5-chloro-4-(2,3-dihydroxypropyl)amino-2-nitrobenzene (CAS 95576-89-9) and for HC Red No.11 1-chloro-2,5-di((2,3-dihydroxypropyl)amino)-4-nitrobenzene (CAS 95576-92-4), earlier called Red Y, has been submitted in March 1992 by COLIPA^{1, 2}.

The Scientific Committee on Cosmetology (SCC) adopted at its 53rd plenary meeting on 25 June 1993 an opinion (SPC/1076/93) with the final conclusion that:

"Red Y was found moderately to slightly toxic in the acute oral toxicity test and slightly toxic after dermal administration to rabbits. Red Y showed no signs of irritation and sensitization. In the 90-day study with rats, 40 mg/kg bw was considered to be the NOAEL. In the teratogenicity study, no irreversible structural changes were observed in the foetuses of the rat, after administration of 30 mg/kg bw. Red Y has mutagenic potential in in vitro assays, but has to be considered as a non-genotoxic in vivo. The cutaneous absorption was 0.037 % of the administered 14C for hair dyeing formulation I, 0.061 % for formulation II and 0.066 % for the solution. For normal use of hair dye, the following calculation can be made: 1 g Red Y comes in contact with the human skin in permanent hair dye condition (based on a usage volume of 100 ml containing maximal 1 % Red Y). With a maximal penetration of 0.061 %, this results in a dermal absorption of 0.61 mg per treatment, which is 0.01 mg/kg bw (assuming a body weight of 60 kg). 0.35 g nitroblau comes in contact with the human skin in semi-permanent hair dye condition (based on a usage volume 35 ml containing maximal 1 % Red Y). With a penetration of 0.037 %; this results in a dermal absorption of 0.129 mg per treatment, which is 0.0022 mg/kg bw. So a margin of safety of 3934 can be calculated between the figure for human exposure to oxidative hair dye and the no adverse level found in rats in the 90-day study. For the semi-permanent hair dye a safety margin of 18532 can be calculated. It should be noted that the NOAEL stems from a daily exposure for 90 days, whereas human exposure to permanent hair dye is unlikely to be more frequent than once a month and human exposure to semi-permanent hair dye is unlikely to be more than once a week."

The "substance" is currently regulated by the Cosmetics Directive (76/768/EC), Annex III, Part 2 under entry 50 on the List of substances, provisionally allowed, which cosmetic products must not contain except subject to restrictions and conditions laid down.

Submission II was submitted in July 2005 by COLIPA. According to this submission HC Red No. 10 + HC Red No. 11 is used as:

- a) a non-reactive hair colouring agent ("direct dye") in non-oxidative hair dye formulations at a maximum on-head concentration of 2.0%. It is common practice to apply 35 to 50 g of the product over a period of 30 minutes followed by rinse off with water and shampoo. The application may be repeated at weekly intervals.
- b) a non-reactive hair colouring agent ("direct dye") in oxidative hair dye formulations at a maximum on-head concentration of 1.0%. The colorant component and a developer (hydrogen peroxide) are mixed in ratios between 1:1 to 1:3. It is common practice to apply up to 100 g of the finished mixed product for a period of 30 minutes followed by rinse off with water and shampoo. The application may be repeated at monthly intervals.

Submission II presents updated scientific data on the above mentioned substance in line with the second step of the strategy for the evaluation of hair dyes

¹ COLIPA - European Cosmetics Toiletry and Perfumery Association

² According to records of COLIPA

(<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 HC Red n° 10 + HC Red n° 11 safe for use as a non-oxidative hair dye with an on-head concentration of maximum 2.0 % taken into account the scientific data provided?*
2. *Does the SCCP consider HC Red No. 10 + HC Red No. 11 safe for use in oxidative hair dye formulations with an on-head concentration of maximum 1.0 % taken into account the scientific data provided?*
3. *Does the SCCP recommend any further restrictions with regard to the use of HC Red n° 10 + HC Red n° 11 in any non-oxidative or oxidative hair dye formulations?*

3. OPINION

3.1. Chemical and Physical Specifications

3.1.1. Chemical identity

3.1.1.1. Primary name and/or INCI name

Mixture of HC Red n° 10 (INCI) and HC Red n° 11 (INCI)

3.1.1.2. Chemical names

HC Red n° 10

- 1-amino-2-nitro-4-(2',3'-dihydroxypropyl)amino-5-chlorobenzene
- 1,2-Propanediol, 3-[(4-amino-2-chloro-5-nitrophenyl)amino]-, (CA, Index name, 9CI)
- 3-(4-Amino-2-chloro-nitroanilino)-1,2-propanediol (IUPAC)
- 1-Amino-5-chloro-4-(2,3-dihydroxypropyl)amino-2-nitrobenzene

HC Red n° 11

- 1,4-bis-(2',3'-dihydroxypropyl)amino-2-nitro-5-chlorobenzene
- 1,2-Propanediol, 3,3'-(2-chloro-5-nitro-1,4-phenylene)diimino]bis-, (CA, Index name, 9CI)
- 1,2-Propanediol, 3,3'-(4-amino-2-chloro-5-nitrophenyl)amino]bis-,
- 1-Chloro-2,5-di[(2,3-dihydroxypropyl)amino]-4-nitrobenzene

3.1.1.3. Trade names and abbreviations

Rubinrot Y

COLIPA B71

Subst. Code: A000692 (HC Red n° 10) and A000865 (HC Red n° 11)

3.1.1.4. CAS / EINECS number

HC Red n° 10

CAS: 95576-89-9
ELINCS: /

HC Red n° 11

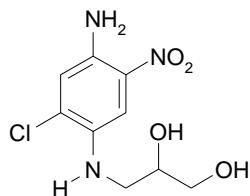
CAS: 95576-92-4
ELINCS: /

Rot Y or Rubinrot Y

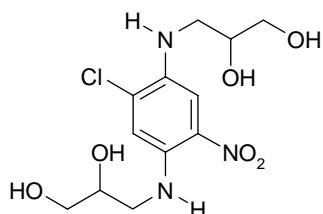
CAS: /
ELINCS: 408-240-1 (1-amino-2-nitro-4-(2',3'-dihydroxypropyl)amino-5-chlorobenzene and 1,4-bis-(2',3'-dihydroxypropyl)amino-2-nitro-5-chlorobenzene)

3.1.1.5. Structural formula

HC Red n° 10



HC Red n° 11



3.1.1.6. Empirical formula

HC Red n° 10: C₉H₁₂CIN₃O₄

HC Red n° 11: C₁₂H₁₈CIN₃O₆

3.1.2. Physical form

Red brown powder

3.1.3. Molecular weight

HC Red n° 10: 261.67

HC Red n° 11: 335.74

3.1.4. Purity, composition and substance codes

Purity HC Red n° 10 (HPLC 254 nm): 58-66%, area

Content HC Red n° 10 (HPLC): 51-54%, w/w (batch LEH5/1 is an exception with 40.3%, w/w)

Purity HC Red n° 11 (HPLC 254 nm): 24-40%, area

Content HC Red n° 11 (HPLC): 32-39%, w/w (batch LEH5/1 is an exception with 19.3%, w/w)

Lot n° H113/4193 arrival n° 967195,

Purity (declared): 66% HC Red n° 10, 33% HC Red n° 11, maximum 6% water and inorganic salts

Purity (found): 65.5% HC Red n° 10, 30.4% HC Red n° 10

3.1.5. Impurities / accompanying contaminants

Solvent content: < 6.3%

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Ash: < 6%

Element screening: in most of the batches, some content of Na, Mg, Si, Ca, Fe, Br and K in small quantities were detected. Only batch LEH5/1 showed a high content of K (2.56%), Fe (492 ppm) and Pb (25 ppm). It was the only batch which contained more than 10 ppm of Pb.

Potential impurities

5-Chloro-2-nitro-p-phenylenediamine: < 1%, w/w

2-Chloro-1,4-diaminobenzene: < 10 ppm (not detected, LOD – 10 ppm)

Chloride: < 2%, w/w

Solvent residues

Solvents, (i.e. solvents such as methanol, ethanol, isopropanol, n-propanol, acetone, ethyl acetate, cyclohexane, methyl ethyl ketone and monochlorobenzene < 100 ppm) were not detected.

Batches used: L4/141 (V07/600pf
LEH5/1
9375 (R00058409)
228-41185
5465 Fass 6/8*

* Batch 5465 Fass 6/8, which was used in two studies (dermal penetration in vitro), is not included in the batch comparison. Since batch 5465 Fass 6/8 was retained from current production material, it was approved to fulfil the internal specification and thus conforms with the other batches listed in table 1.

Table 1: comparison of different batches

Description of sample	L4/141 (V07/600pf)		LEH5/1		9375 (R00058409)		228-41185	
Reference of analyses	G 2005/008		G 2005/008		A 2001/038 G 2005/008		A 2002/247 G 2005/008	
	HC RED 10	HC RED 11	HC RED 10	HC RED 11	HC RED 10	HC RED 11	HC RED 10	HC RED 11
NMR content / %, w/w	55.0	40.2	43.6	21.3	57.2	32.8	53.0	38.6
HPLC purity / area% *								
210 nm	60.0	33.6	65.0	24.2	62.7	33.6	60.9	36.5
254 nm	58.4	37.0	64.5	27.4	62.5	34.9	59.2	38.7
500 nm	58.0	38.5	65.2	29.1	62.2	35.9	59.3	39.5
HPLC content / %, w/w	51.8	35.4	40.3	19.3	53.6	32.3	53.2	38.4
5-Chloro-2-nitro-p-phenylenediamine (Rot C) / %, w/w	0.24		0.48		0.14		0.35	
2-Chloro-1,4-diaminobenzene / ppm	< 10 °		< 10 °		< 10 °		< 10 °	
Chloride	0.07		6.28		negative		***	
Water / % w/w	0.94		1.69		1.66		***	
Loss on dryling / %, w/w	0.37		1.34		2.1		***	
Sulphated ash / %, w/w	0.15		5.95		2.7		***	
Element screening / ppm	Na 369 Mg 25 Si 110 Ca 174 Fe 13 Br 28		Na 896 Si 98 K 25600 Ca 50 Fe 492 Pb 25			***	Na 400 Mg 23 Si 100 Ca 150 Br 21	

* The HPLC content refers to HC RED 10: charge MOR 10/1 (10), 98.7%, w/w (VM0003 = A2001/038-002; HC RED 11: charge MOR 10/2 (6) and (5), 99.4%, w/w (VM0004 = A2001/038-003)

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** HPLC conditions: Merck Purospher RP-18e, 125-3-5, Eluent: ACN + buffer (0.02 M KH₂PO₄, pH 3.2); Gradient; 0-4 min ACN:buffer 2:8; 9-16 min ACN:buffer 5:5; 21-30 min ACN:buffer 2:8; flow: 0.5 ml/min
 *** Not determined because lack of substance
 o Not detected, shown value indicates limit of detection

Deduced specification for B71

Purity HC RED 10 (HPLC 254 nm): 55 – 70%, area
 Purity HC RED 11 (HPLC 254 nm): 30 – 40%, area
 5-Chloro-2-nitro-p-phenylenediamine: < 1%, w/w
 Solvent content (water): < 5%
 Ash: < 3%

3.1.6. Solubility

Water: 0.5 < S < 6 g/l
 DMSO: > 100 g/l
 Ethanol: 40 < S < 80 g/l

3.1.7. Partition coefficient (Log P_{ow})***HC RED 10***

P_{ow}: 10.23
 Log P_{ow}: 1.01

HC RED 11

P_{ow}: 1.028
 Log P_{ow}: 0.012

pH: 7.5 at 25 °C
 Ref.: 1

Mean P_{ow}: 7.16 (calculated)
 Mean Log P_{ow}: 0.012 (calculated)

After experimental determination for the single components, the mean P_{ow} and mean Log P_{ow} were calculated for a 2:1 ratio of HC RED 10 and HC RED 11 respectively.

3.1.8. Additional physical and chemical specifications

pH:	7.3 (saturated aqueous solution, 22 °C)	(ref. 2)
Melting range:	109.8 - 111.8 °C	(OECD 102) (ref. 3)
Boiling point:	252.9 °C (decomposition)	(OECD 103) (ref. 4)
Density:	1.53 g/cm ³ (25 °C)	(OECD 109) (ref. 5)
Vapour pressure:	13.9 hPa (25 °C)	(OECD 104) (ref. 6)
Surface tension (in water):	72.7 mN/m (26.2 °C)	(EU - A.5) (ref. 7)
Water solubility:	2175.6 mg/l (22 °C)	(EU - A.6) (ref. 2)
Flammability (solids):	not highly flammable	(EU - A.10) (ref. 8)
Explosive properties:	not explosive	(EU - A.14) (ref. 9)
Relative self-ignition temp.:	> 400 °C	(EU - A.16) (ref. 10)
Oxidising properties:	not oxidising	(EU - A.17) (ref. 11)

3.1.9. Stability

No specific data on stability was provided. However, in the dermal absorption studies, it was mentioned that the test substance was stable for more than 7 days.

General Comments to physico-chemical characterisation

- * The composition of this hair dye appears to be variable, depending on the yield of the synthetic process as indicated by the variable range for each of the two component hair dyes, with extreme case the Batch LEH5/1 ($a=40.3\%$, $b=19.3\%$) considered as "an exception".
- * The sum of components reported for the Batch LEH5/1 is about 79-80 %. Hence, about 20% of its content is totally unknown.
- * Physical constants such as melting point, solubility etc. for a mixture of chemical (and of variable composition) are inadequate especially in the absence of respective figures for each component. The same is true for the calculated mean Log P_{ow} for the mixture.

3.2. Function and uses

a) Semipermanent Hair Colorants

HC Red n° 10 + HC Red n° 11 is used as a non-reactive hair colouring agent ("Direct Dye") in semipermanent hair dye formulations at a maximum on-head concentration of 2%.

b) Oxidative Hair Colorants

HC Red n° 10 + HC Red n° 11 is used as a non-reactive hair colouring agent ("Direct Dye") in oxidative hair dye formulations at a maximum on-head concentration of 1%.

3.3. Toxicological Evaluation

A toxicological evaluation of HC Red n° 10 and HC Red n° 11 is not feasible since there is a high variability in the mixtures of HC Red n° 10 and HC Red n° 11 used.

In addition, HC Red n° 10 and HC Red n° 11 have different physico-chemical properties as seen by the partition coefficient (HC Red n° 10: P_{ow} of 10.2 and Log P_{ow} of 10.2; HC Red n° 11: P_{ow} of 1.028 and Log P_{ow} of 0.012). These affect the bioavailability/behaviour of the two compounds of the mixture. This is seen in the toxicokinetic study (permeability in human intestinal epithelial (TC-7) cells), where the apparent permeability coefficient (P_{app}) of HC Red n° 10 was 55.5×10^{-6} cm/sec, whereas P_{app} for HC Red n° 11 was 0.2×10^{-6} cm/sec. HC Red n° 10 is classified as having high permeability whilst HC Red n° 11 is classified as having low permeability.

3.3.1. Acute toxicity

Not applicable

3.3.2 Irritation and corrosivity

Not applicable

3.3.3. Skin sensitisation

Not applicable

3.3.4. Dermal / percutaneous absorption

Not applicable

3.3.5. Repeated dose toxicity

Not applicable

3.3.6. Mutagenicity / Genotoxicity

Not applicable

3.3.7. Carcinogenicity

Not applicable

3.3.8. Reproductive toxicity

Not applicable

3.3.9. Toxicokinetics

Not applicable

3.3.10. Photo-induced toxicity

Not applicable

3.3.11. Human data

Not applicable

3.3.12. Special investigations

Not applicable

3.3.13. Safety evaluation (including calculation of the MoS)**CALCULATION OF THE MARGIN OF SAFETY**

Not applicable

3.3.14. Discussion

Not applicable

4. CONCLUSION

The mixture of HC Red n° 10 + HC Red n° 11 (COLIPA B71) is highly variable with the two compounds having different physico-chemical properties which possibly also affect toxicological properties.

Consequently, the SCCP is not in a position to perform a risk assessment of HC Red n° 10 + HC Red n° 11 because of the absence of a proper chemical characterisation of the test substance.

5. MINORITY OPINION

Not applicable

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