



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL
Directorate C – Public Health and Risk Assessment
C7 Risk assessment
Scientific Committee on Consumer Products

SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS
10TH PLENARY MEETING

Held on 19 December 2006 in Brussels

MINUTES

1. WELCOME AND APOLOGIES

Dr. I.R. White welcomed all the participants. Apologies were received from Dr. C. Chambers, Prof. R. Dubakiene, Prof. G. Degen, Dr. R. Grimalt, Dr. B. Jazwicz-Kanyion and Prof. J. Krutmann.

2. DECLARATION OF INTEREST ON MATTERS ON THE AGENDA

No member declared any interest that could prevent him/her from participating in the discussion of the items on the agenda.

3. APPROVAL OF THE AGENDA

The draft agenda was approved.

4. APPROVAL OF THE MINUTES OF THE 9TH PLENARY MEETING

Minutes of the 9th plenary meeting were approved.

5. INFORMATION FROM CHAIRMAN/MEMBERS

Dr. White said that because of the establishment of the European Chemicals Agency in Helsinki, the Commission decided to prolong the terms of office for the current members of the three Scientific Committees until the end of 2008. The members will be asked whether they would remain in office or whether they prefer to resign. If needed, the Commission will launch a limited Call for Experts to replace the resigning members.

Also, Dr. White informed the members about the forthcoming Risk Assessment Days, organized by DG SANCO on 21 and 22 March 2007. The overall aim of this event is to raise awareness of DG SANCO Scientific Committees' activities. Discussions are foreseen with members of the European Parliament and stakeholders.

Finally, he reported on 2nd meeting of the Chairs of the Scientific Committees of Community Bodies involved in Risk Assessment (24-25 October 2006).

6. EMERGING ISSUES

No issues were raised.

7. DISCUSSION AND POSSIBLE ADOPTION OF A SCIENTIFIC OPINION

The adopted opinions will be published at:

http://europa.eu.int/comm/health/ph_risk/committees/04_sccp/sccp_opinions_en.htm

7.1. ALTERNATIVES

Report of the Co-ordinator

Prof. Rogiers presented the 6th revision of the Notes of Guidance. The main changes concern an update of:

- the recommended strategy for testing hair dyes for their potential genotoxicity/mutagenicity/carcinogenicity (see also doc. n° SCCNFP/0720/03, and of
- the basic criteria for the *in vitro* assessment of dermal absorption of cosmetic ingredients (see also doc. n° SCCP/0970/06).

The document was adopted.

7.2. HAIR DYES AND COLORANTS

Report of the Co-ordinator

Prof. T. Platzek reported on the work done during the meetings of the WG that had taken place since the last plenary of 10 October 2006.

Draft opinions were prepared on:

A9, N-Phenyl-p-phenylenediamine, doc. n° SCCP/0991/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider N-Phenyl-p-phenylenediamine safe for use in oxidative hair dye formulations up to a concentration of 0.2% on the head taken into account the scientific data provided?*
2. *Does the SCCP recommend any restrictions with regard to the use of N-Phenyl-p-phenylenediamine in oxidative hair dye formulations besides the existing labelling requirements for allergic reactions?*

The SCCP concluded that a proper NO(A)EL for subchronic toxicity cannot be set due to the shortcomings of the experimental data provided.

Data is required to meet modern guidelines with special attention to the effects on fertility together with reproductive parameters. The current lack of data on the effects of N-Phenyl-p-phenylenediamine on females needs to be addressed since maternotoxicity was seen in the developmental studies. In addition, liver effects were noted in males.

In the male, fertility seems to be compromised with signs of testicular toxicity (arrested spermatogenesis and maturation of spermatocytes) signalled by significantly reduced enzyme levels implying reduced energy availability during spermatogenesis.

The substance has shown to be an extremely potent skin sensitiser.

N-phenyl-p-phenylenediamine itself has no mutagenic potential *in vivo*.

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.

The opinion was adopted.

A15, m-Aminophenol, doc. n° SCCP/0978/06
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The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider m-Aminophenol safe for use as an oxidative hair dye with an on-head concentration of maximum 1.2 % taken into account the scientific data provided?*
2. *Does the SCCP recommend any further restrictions with regard to the use of m-Aminophenol in oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of m-aminophenol itself as an oxidative hair dye substance at a maximum concentration of 1.2% in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential.

m-Aminophenol itself has no mutagenic potential *in vivo*.

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.

The opinion was adopted.

A39, Phenyl methyl pyrazolone, doc. n° SCCP/1033/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider phenyl methyl pyrazolone safe for use as an oxidative hair dye with a concentration on the head of maximum 0.25 % taken into account the scientific data provided?*
2. *Does the SCCP recommend any restrictions with regard to the use of phenyl methyl pyrazolone in oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of phenyl methyl pyrazolone itself as an oxidative hair dye substance at a maximum concentration of 0.25% in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential.

Phenyl methyl pyrazolone itself is not mutagenic *in vivo*.

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.

The opinion was adopted.

A99, 2,6-Dihydroxy-3,4-dimethylpyridine, doc. n° SCCP/1034/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 2,6-Dihydroxy-3,4-dimethylpyridine safe for use as an ingredient in both oxidative and non-oxidative hair dye formulations with a concentration on the scalp of maximum 1.0% taking into account the scientific data provided?*
2. *Does the SCCP have any other concerns with regard to the use of 2,6-Dihydroxy-3,4-dimethylpyridine in both oxidative hair dyes and non-oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of 2,6-Dihydroxy-3,4-dimethylpyridine itself as an oxidative hair dye substance at a maximum concentration of 1.0% in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential.

2,6-Dihydroxy-3,4-dimethylpyridine itself is not mutagenic *in vivo*.

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.

The opinion was adopted.

A121, Hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine) HCl, doc. n° SCCP/1051/06
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The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 1,3-Bis[(4-aminophenyl)-(2-hydroxyethyl)-amino]-propan-2-ol tetrahydrochloride safe for use in oxidative hair dye formulations up to a concentration of 1.5% on the head taken into account the scientific data provided?*
2. *Does the Scientific Committee on Consumer Products (SCCP) recommend any further restrictions with regard to the use of 1,3-Bis[(4-aminophenyl)-(2-hydroxyethyl)-amino]-propan-2-ol tetrahydrochloride in hair dye formulations?*

The SCCP concluded that, based on the toxicity of hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine) in a sub-chronic oral rat study (at the lowest systemic dose level of 1.25 mg/kg bw/day derived from toxicokinetic data) and the estimated human exposure (highest value calculated from in vitro-experiments on percutaneous absorption: 0.04 mg/kg bw), the margin of exposure is considered too low for a safe use of this substance in hair dye formulations.

The substance is a strong sensitiser in the Guinea pig.

The opinion was adopted.

B24, 4-Nitro-o-phenylenediamine, doc. n° SCCP/0980/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 4-Nitro-o-phenylenediamine safe for use as an oxidative hair dye with an on-head concentration of maximum 0.5 % taken into account the scientific data provided?*
2. *Does the SCCP recommend any further restrictions with regard to the use 4-Nitro-o-phenylenediamine in oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of 4-Nitro-o-phenylenediamine itself as an oxidative hair dye substance at a maximum concentration of 0.5% in the finished cosmetic product (after mixing with hydrogen peroxide) does not pose a risk to the health of the consumer, apart from its sensitising potential.

4-Nitro-o-phenylenediamine itself is not genotoxic *in vivo*.

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.

The opinion was adopted.

B37, HC Blue n° 2, doc. n° SCCP/1035/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider HC Blue n° 2 safe for use as a non-oxidative hair dye with a concentration of maximum 2.8 % taken into account the scientific data provided?*

2. *Does the SCCP recommend any further restrictions with regard to the use HC Blue n° 2 in non-oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of HC Blue n° 2 itself in semi-permanent hair dye formulations at a maximum concentration of 2.8% in the finished cosmetic product does not pose a risk to the health of the consumer, apart from its sensitising potential.

However, HC Blue n° 2 is comprised of both a secondary and a tertiary amino group, and thus is prone to nitrosation. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

The opinion was adopted.

B54, 3-Nitro-p-hydroxyethylaminophenol, doc. n° SCCP/1036/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 3-nitro-p-hydroxyethylaminophenol safe for use as an ingredient in both oxidative hair dyes and non-oxidative hair dye formulations with a concentration on-head of maximum 3.0% respectively 1.85% taking into account the scientific data provided?*
2. *Does the SCCP recommend any restrictions with regard to the use of 3-nitro-p-hydroxyethylaminophenol in both oxidative hair dyes and non-oxidative hair dye formulations?*

The SCCP concluded that, based on the information provided, the use of 3-nitro-p-hydroxyethylaminophenol itself as an oxidative hair dye substance at a maximum concentration of 3.0% in the finished cosmetic product (after mixing with hydrogen peroxide) or as an ingredient in semi-permanent hair colouring products at a maximum concentration of 1.85% does not pose a risk to the health of the consumer, apart from its sensitising potential.

3-Nitro-p-hydroxyethylaminophenol is a secondary amine, and thus is prone to nitrosation. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

3-Nitro-p-hydroxyethylaminophenol itself is not mutagenic *in vivo*.

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.

The opinion was adopted.

Memorandum on hair dye substances and their skin sensitising properties, doc. n° SCCP/1054/06

Contact allergy and allergic contact dermatitis caused by hair dyes is an important and increasing health problem to consumers and society, often causing acute and severe dermatitis on the face, scalp and neck.

Until now, the SCCP and the former SCCNFP opinions on substances, for which the dossiers submitted by industry have been assessed, have largely concerned the general toxicology of the substances, albeit there has been a statement regarding sensitising potential. Of the adopted opinions on 46 hair dye substances, 10 of these substances were categorised as extreme, 13 as strong and 4 as moderate skin sensitisers, all fulfilling the EU criteria for classification as a skin sensitiser (R43).

The SCCP wishes to state that hair dye substances which fulfil the criteria for classification as R43, may not be safe for consumers. This is particularly so for hair dye substances categorised as extreme and strong skin sensitisers.

Market surveys in Europe, the USA and in Japan, indicate that hair dyeing has become much more prevalent during the last ten years, that it is done at a younger age and that the proportion of men is increasing.

The objective of this memorandum is to draw the attention of the Commission to the fact that many of currently used hair dye substances are skin sensitisers, and that this property may be of concern for the health of consumers.

The memorandum is attached to these minutes.

7.3. PRESERVATIVES AND FRAGRANCES

Report of the Co-ordinator

Dr. White said that the following opinion had been prepared:

Methyl-N-methylantranilate, doc. n° SCCP/1068/06
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The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of Methyl-N-methylantranilate to be safe for the consumers, when used as an ingredient in perfumes in leave-on products in a concentration less than 0.1 % in the finished cosmetic product taking into consideration the provided data?*
2. *Does SCCP recommend any restrictions in the use of Petitgrain Mandarin oil due to its content of Methyl-N-methylantranilate in cosmetic products?*
3. *Does SCCP recommend any restriction for the use of the substance in rinse-off products?*

The SCCP concluded that methyl-N-methylantranilate is phototoxic as demonstrated by both *in vivo* and *in vitro* experiments. Although the action spectrum of the phototoxicity has not been provided, phototoxicity is normally within the UVA spectrum.

The lowest NOAEL in humans was at 0.1% with 16 J UVA/cm² (with 0.75 MED UVB) (ref 34768). However, an *in vitro* test indicated that it was phototoxic at 0.05%, the lowest dilution tested (ref 9196). Phototoxicity is related to the product of dose and UV exposure.

Because of the phototoxicity, methyl-N-methylantranilate should not be deliberately added to leave-on cosmetic products, as there is always the potential for light exposure.

Until appropriate toxicity data on the substance are available, including information on the possible nitrosamine formation by this secondary amine, up to 0.1% can be used in rinse-off finished cosmetic products.

The above opinion applies also to the presence of methyl-N-methylantranilate in essential oils, including Petitgrain Mandarin.

The opinion was adopted.

7.4. UV FILTERS AND AD HOC SUBSTANCES

Prof. Sanner said that the following opinions had been prepared:

DEGBE, doc. n° SCCP/1043/06

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of DEGBE as solvent in hair dyes in a concentration up to 9% safe for the consumer, taken into consideration the scientific data provided?*
2. *If not, does the SCCP foresee any other restrictions to the safe use of DEGBE?*

The SCCP concluded that, based on the information provided, the use of diethylene glycol monobutyl ether (DEGBE) as a solvent in hair dye formulations at a concentration up to 9.0% does not pose a risk to the health of the consumer.

The opinion relates to the direct application to the hair/scalp. It does not include any other cosmetic exposure, such as exposure from other types of cosmetics or possible aerosol/spray products.

The opinion was adopted.

DEGEE, doc. n° SCCP/1044/06

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of DEGEE in all cosmetics except product for oral hygiene in a concentration up to 1.5% safe for the consumer taken into consideration the scientific data provided?*
2. *If not, does the SCCP foresee any other restrictions to the safe use of DEGEE?*

The SCCP concluded that, based on the information provided, the use of diethylene glycol monoethyl ether (DEGEE) in all cosmetic products, except products for oral hygiene and eye products at a concentrations up to 1.5% does not pose a risk to the health of the consumer, provided that the level of ethylene glycol in DEGEE used is < 0.2%.

The opinion relates to the dermal application. It does not include any other cosmetic exposure, such as exposure from possible aerosol/spray products.

The opinion was adopted.

S38, Benzophenone-3, doc. n° SCCP/1069/06

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of 2-hydroxy-4-methoxybenzone in a concentration up to 10% w/w in sunscreen products safe for the consumer?*
2. *Does the SCCP consider the use of 2-hydroxy-4-methoxybenzone in a concentration up to 10% w/w in other products than sunscreen products safe for the consumer?*
3. *Does the SCCP foresee any other restrictions to the safe use of 2-hydroxy-4-methoxybenzone?*

The SCCP concluded that insufficient data were presented to calculate the Margin of Safety of Benzophenone-3 under the proposed conditions of use.

The following additional information is required:

- A dermal absorption study with Benzophenone-3 under its in-use concentrations (up to 10%) according to OECD Guideline 428 combined with SCCP/0970/06.

These data are requested before end of March 2007.

The opinion was adopted.

S45, Phenylbenzimidazole sulfonic acid and its salts, doc. n° SCCP/1056/06
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The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of 2-Phenylbenzimidazole-5-sulfonic acid and its salts in a concentration up to 8% w/w in sunscreen products safe for the consumer?*
2. *Does the SCCP consider the use of 2-Phenylbenzimidazole-5-sulfonic acid and its salts in a concentration up to 8% w/w in other products than sunscreen products safe for the consumer?*
3. *Does the SCCP foresee any other restrictions to the safe use of 2-Phenylbenzimidazole-5-sulfonic acid and its salts?*

The SCCP concluded that, based on the information provided, the use of phenylbenzimidazole sulfonic acid and its salts as a UV-filter at a maximum concentration of 8.0% in the cosmetic sun protection preparations does not pose a risk to the health of the consumer.

Uses of phenylbenzimidazole sulfonic acid and its salts in other types of cosmetic products at concentrations up to 8.0% also do not pose a risk to the health of the consumer.

The opinion was adopted.

S57, Camphor benzalkonium methosulfate, doc. n° SCCP/1015/06

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of Camphor benzalkonium methosulfate in a concentration up to 6% w/w in sunscreen products safe for the consumer?*
2. *Does the SCCP consider the use of Camphor benzalkonium methosulfate in a concentration up to 6% w/w in other products than sunscreen products safe for the consumer?*
3. *Does the SCCP foresee any other restrictions to the safe use of Camphor benzalkonium methosulfate?*

The SCCP concluded that, based on the information provided, the use of camphor benzalkonium methosulphate as a UV-filter at a maximum concentration of 6.0% in the cosmetic sun protection preparations does not pose a risk to the health of the consumer.

Because of its borderline Margin of Safety, its use in other types of cosmetic products is not recommended. However, this figure does include the outlier which may or may not be relevant.

A new study on dermal absorption following the relevant SCCNFP opinions and in accordance with its Notes of Guidance is required before any reconsideration of the opinion.

The opinion was adopted.

ETH50

This novel UV filter was assessed for its possible use in sun screen products. The SCCP concluded that the information submitted was insufficient to allow a final risk assessment to be carried out.

As the dossier was submitted under the confidentiality clause, the full report cannot be published.

8. NEXT PLENARY MEETING

The 11th plenary meeting of the SCCP will take place on 21 March 2007.

9. ANY OTHER BUSINESS

- Dates of WG meetings:

9 January Hair Dyes

Minutes of the 10th plenary meeting of the SCCP of 19 December 2006

16 January	Nano-substances in Cosmetics
30 January	Hair Dyes
6 February	Nano-substances in Cosmetics
13 February	ad hoc substances + Fragrances & Preservatives
20 February	Hair Dyes
28 February	Nano-substances in Cosmetics
6 March	ad hoc substances + Fragrances & Preservatives
13 March	Hair Dyes
14 March	Nano-substances in Cosmetics

Annex I: List of Participants.

Annex II: Memorandum on hair dye substances and their skin sensitising properties

Annex I

Scientific Committee on Consumer products 9 th Plenary Meeting
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Held on 10 October 2006
in Brussels

List of Participants**Members of the SCCP**

Prof. V. KAPOULAS, Prof. C. LIDÉN, Prof. J.-P. MARTY, Prof. T. PLATZEK, Dr. S. RASTOGI, Prof. J. REVUZ, Prof. V. ROGIERS (Vice chair), Prof. T. SANNER (Vice chair), Prof. G. SPEIT, Dr. J. VAN ENGELEN, Dr. I.R. WHITE (Chair)

SCCP Secretariat (DG SANCO)

Mrs. C. DEKINDT, Mr. B. DELOGU, Mrs. T. PEETSO, Mrs M. PUOLAMAA, Mr. A. VAN ELST

DG ENTR F3: Mrs. A. ORLOFF



Scientific Committee on Consumer Products

SCCP

MEMORANDUM ON

HAIR DYE SUBSTANCES AND THEIR SKIN SENSITISING PROPERTIES

The SCCP adopted this memorandum during its 10th plenary of 19 December 2006

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 (EMA), 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.

Scientific Committee members

Claire M. Chambers, Gisela Degen, Ruta Dubakiene, Ramon Grimalt, Bozena Jazwicz-Kanyion, Vassilios Kapoulas, Jean Krutmann, Carola Lidén, Jean-Paul Marty, Thomas Platzek, Suresh C. Rastogi, Jean Revuz, Vera Rogiers, Tore Sanner, Günter Speit, Jacqueline van Engelen, Ian R. White

Contact:

European Commission
Health & Consumer Protection DG
Directorate C: Public Health and Risk Assessment
Unit C7 - Risk Assessment
Office: B232 B-1049 Brussels

Sanco-Sc6-Secretariat@ec.europa.eu

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The opinions of the Scientific Committees reflect the views of the independent scientists who are members of the committees. They do not necessarily reflect the views of the European Commission. The opinions are published by the European Commission in their original language only.

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

1. ACKNOWLEDGEMENTS

Members of the working group are acknowledged for their valuable contribution to this opinion. The members of the working group are:

Dr. C. Chambers
Prof. V. Kapoulas
Prof. C. Lidén (rapporteur)
Prof. J.-P. Marty
Prof. T. Platzek (chairman)
Dr. S.C. Rastogi
Prof. T. Sanner
Dr. J. van Engelen
Dr. I.R. White

Keywords: SCCP, memorandum, hair dye, skin sensitisation, Directive 768/76/EEC6

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2. BACKGROUND

In view of particular safety concerns expressed in relation to the use of some hair dyes, the Commission agreed in April 2003 together with Member States and the stakeholders, on an overall detailed strategy to regulate hair dye substances within the framework of the Cosmetics Directive (4, 7).

Industry has submitted dossiers on 117 different hair dye substances used in hair dye products. Because of missing dossiers the Commission has recently banned 22, and is in process of acting on others. The potential risk of cancers, genotoxicity or mutagenicity caused by use of certain hair dye substances has raised much concern. The fact that a number of hair dye substances are well-known skin sensitisers has, however, not drawn much attention, until now.

p-Phenylenediamine and related compounds have, for more than 100 years, been used in permanent hair dyes, and more than two thirds of hair dyes currently used contain p-phenylenediamine. p-Phenylenediamine is a well-known and potent skin sensitiser. Scientific reporting and clinical diagnosis in patients with dermatitis from hair dyes have focused on p-phenylenediamine as the main skin sensitiser. p-Phenylenediamine 1% in petrolatum is used in the European standard series for diagnostic patch testing in patients with eczematous skin conditions. Knowledge among dermatologists about the use of other hair dye substances, and access to these for patch testing, are limited. Testing with p-phenylenediamine alone may fail to detect contact allergy to relevant hair dye substances (3, 17).

Several studies in Europe (UK, Germany, Belgium, Portugal) and in Asia (Thailand, Japan, Singapore) show that contact allergy to p-phenylenediamine has increased significantly in the general population and in hairdressers over the last decades. It has been estimated that up to 1.3 million adults in Germany may be sensitive to p-phenylenediamine. (2, 8, 9, 13, 15, 18-20)

In a consumer complaint-based data analysed for persons who reported adverse reactions to hair dyes, 55 cases of severe, acute allergic contact dermatitis were identified. The clinical picture was severe oedema of the face, scalp and ears, clinically often mistaken for angio-oedema. Admissions to hospital and sick leave were reported, which indicate very severe dermatitis (16).

Market surveys in Europe, the US and in Japan, indicate that hair dyeing has become much more prevalent during the last ten years, that it is done at a younger age and that the proportion of men is increasing (9). In Denmark, 75% of women and 18% of men reported that they have used hair dye; the median age at first hair dyeing was 16 years (18).

The objective of this memorandum is to draw the attention of the Commission to the fact that many of currently used hair dye substances are skin sensitisers, and that this property may be of concern for the health of consumers.

3. CLASSIFICATION AND CATEGORISATION OF SKIN SENSITISERS

The animal test methods used in harmonised classification of substances, according to their potential to cause skin sensitisation, are the guinea pig maximisation test (GPMT), the Buehler test, and the local lymph node assay (LLNA) (11, 12). These methods are used in hazard identification and risk assessment for regulatory purpose (Directives on Dangerous Substances 67/548/EEC, Dangerous Preparations 1999/45/EC). As yet, there is not a validated *in vitro* test method accepted for skin sensitisation. Therefore, also for cosmetic

ingredients the LLNA, the GPMT and the Buhler test are used in accordance with the Cosmetics directive 76/768/EEC and the SCCP Notes of Guidance (14).

According to Directives 67/548/EEC and 1999/45/EC, substances and preparations shall be classified as sensitising and assigned the symbol "Xi", and the risk phrase "R43 May cause sensitisation by skin contact". Positive results from OECD guideline animal tests (11, 12) sufficient to classify a substance with R43 are:

- GPMT: if at least 30% of the animals have a positive response.
- Buehler test: if at least 15% of the animals have a positive response
- LLNA: if at least a 3-fold increase in proliferative counts is induced, compared to vehicle-treated controls (stimulation index SI ≥ 3).

Further categorisation of substances classified with R43 into three groups according to allergen potency (extreme, strong and moderate) has been proposed (1, 5, 6, 10). Such categorisation is based on EC3 values in the LLNA (Table 1), on intradermal induction concentration in the GPMT (Table 2), and topical induction concentration in the Buehler test (Table 3). When EC3 values are available from more than 1 study, the lowest value should normally be used. Where multiple animal data sets lead to different categorisation of the same substance, the higher potency category should apply (1, 5, 6).

Table 1: Potency categorisation of substances classified with R43, based on the local lymph node assay (LLNA) (1, 6)

Category	EC3 value (%) ^{a)}
Extreme	≤ 0.2
Strong	$> 0.2 - \leq 2$
moderate	> 2

^{a)} EC3 value = the estimated concentration of a chemical necessary to give a 3-fold increase in lymph node cell proliferative activity compared to vehicle-treated controls (SI ≥ 3).

Table 2: Potency categorisation based on the guinea pig maximisation test (GPMT) (1, 6)

Intradermal concentration employed during induction phase (%) ^{a)}	Incidence of sensitisation (30-<60%)	Incidence of sensitisation ($\geq 60\%$)
≤ 0.1	Strong	Extreme
$> 0.1 - \leq 1$	Moderate	Strong
> 1	Moderate	Moderate

^{a)} According to guideline, intradermal induction concentration must be the highest concentration causing mild to moderate irritation.

Table 3. Potency categorisation based on Buehler test (1, 6)

Concentration employed during induction phase (%) ^{a)}	Incidence of sensitisation (15-<60%)	Incidence of sensitisation ($\geq 60\%$)
≤ 0.2	Strong	Extreme
$> 0.2 - \leq 20$	Moderate	Strong
> 20	Moderate	Moderate

^{a)} According to guideline, the topical induction concentration must be the highest concentration causing mild but not excessive irritation.

4. HAIR DYES AND THEIR SKIN SENSITISING POTENTIAL

The safety of hair dye substances is being assessed by the SCCP, based on documentation submitted by industry, including scientific publications and reports by industry on animal sensitisation tests. The SCCP and the former SCCNFP have, until now, assessed the dossiers of 46 of the 117 hair dye substances of interest to industry regarding their skin sensitising property (Table 4).

In Table 4, the hair dye substances are classified according to the abovementioned classification criteria. Substances fulfilling the criteria for classification with R43, are further categorised as extreme, strong and moderate skin sensitisers (1, 6, 10).

In summary, 27 of the 46 hair dye substances assessed by the SCCP fulfil the EU criteria for classification as skin sensitiser (R43). Further categorisation of skin sensitising potency, shows that 10 of the 27 classifiable hair dye substances are extreme sensitisers, 13 are strong, and 4 are moderate sensitiser.

Table 4. Hair dye substances assessed by the SCCP and the former SCCNFP concerning their skin sensitising property, based on submissions by industry. Results from studies performed by OECD guideline methods (LLNA, GPMT, Buehler test). Typically, results from one study per method are displayed. The substances fulfilling the criteria for classifications as skin sensitiser (R43) were categorised according to their sensitising potency (1, 6, 10)

COLIPA N°	Substance	Sensitising potency category	LLNA		GPMT		Buehler test		SCCP/SCCNFP opinion (doc. no.)
			EC3 value (%)	category	i.d. ind./incid.	category	t. ind./incid.	category	
A7	p-Phenylenediamine	extreme	0.06	extreme	-	-	-	-	SCCP/0989/06
A9	N-Phenyl-p-phenylenediamine	extreme	0.02	extreme	-	-	-	-	SCCP/0991/06
A33	1,2,4-Trihydroxybenzene	extreme	0.08	extreme	-	-	-	-	SCCP/0962/05
A111	Dihydroxyindole	extreme	0.17	extreme	0.1/0	not classifiable	-	-	SCCP/0952/05
A128	6-Hydroxyindole	extreme	<0.2 b); 0.2	extreme	0.5/40	moderate	5/30	moderate	SCCP/0947/05
A129	Isatin	extreme	<1 b); 2.5	strong; moderate	0.1/100	extreme	25/0 f)	not classifiable	SCCP/0876/05
B7	Basic Brown 17	extreme	n.v.	not classifiable	0.1/70 d.g)	extreme g)	-	-	SCCP/0683/03
B24	4-Nitro-o-phenylenediamine	extreme	≤0.05	extreme	-	-	-	-	SCCP/0980/06
B48	HC Red n° 1	extreme	<2 a)	strong	0.1/100	extreme	-	-	SCCP/0981/06
B54	3-Nitro-p-hydroxyethylaminophenol	extreme	0.07	extreme	-	-	-	-	SCCP/1036/06
A15	m-Aminophenol	strong	0.24	strong	-	-	-	-	SCCP/0978/06
A27	4-Amino-2-hydroxytoluene	strong	0.44	strong	-	-	-	-	SCCP/1001/06
A39	Phenyl methyl pyrazolone	strong	≤1	strong	-	-	-	-	SCCP/1033/06
A50	N,N-bis(2-hydroxyethyl)-p-phenylenediamine sulfate	strong	<0.25 b); 1.04	strong	-	-	-	-	SCCP/0983/06
A74	4-Amino-m-cresol	strong	1.45	strong	-	-	-	-	SCCP/0898/05
A98	Hydroxyethyl-3,4-methylenedioxyaniline HCl	strong	<0.5 b)	strong	-	-	-	-	SCCP/0951/05
A101	2,6-Dimethoxy-3,5-pyridinediamine HCl	strong	1.25	strong	1/15 f)	not classifiable	-	-	SCCP/0908/05
A121	Hydroxypropyl bis(N-hydroxyethyl-p-phenylenediamine)HCl	strong	-	-	1/90	strong	-	-	SCCP/1051/06
A154	1-Hydroxyethyl-4,5-Diamino Pyrazole Sulfate	strong	-	-	1/100	strong	40/25	moderate	SCCP/0990/06
B66	HC Violet n° 1	strong	0.9	strong	25/0 f)	not classifiable	-	-	SCCP/1025/06
B99	2-Amino-6-chloro-4-nitrophenol	strong	0.68	strong	-	-	-	-	SCCP/0948/05
C117	Hydroxyanthraquinone-aminopropyl Methyl Morpholinium Methosulfate	strong	-	-	0.875/90	strong	26.3/45 8.65/47	moderate	SCCP/0875/05
C146	Lawsone	strong	-	-	1/65 f)	strong	-	-	SCCNFP/0798/04
A22	p-Methylaminophenol sulphate	moderate	2.2	moderate	-	-	-	-	SCCP/0963/05
A42	2,4-Diaminophenoxyethanol and its salts	moderate	3.2	moderate	-	-	100/10	not classifiable	SCCP/0979/06
A44	2-Methylresorcinol	moderate	50	moderate	-	-	-	-	SCCP/1002/06
A147	Dihydroxyindoline HBr	moderate	-	-	10/55	moderate	40/0	not classifiable	SCCNFP/0669/03
A25	Hydroxybenzomorpholine	not classifiable	-	-	1/0	not classifiable	-	-	SCCP/0965/05
A31	2-Methyl-5-hydroxyethylaminophenol	not classifiable	n.v.	not classifiable	-	-	-	-	SCCP/0957/05
A84	2-Amino-4-hydroxyethylaminoanisol sulfate	not classifiable	n.v. c)	not classifiable	-	-	-	-	SCCP/0958/05)
A157	Quinolinium, 4-formyl-1-methyl-, salt	not classifiable	n.v.	not classifiable	-	-	50/0 h)	not classifiable	SCCP/0923/05

MEMORANDUM ON HAIR DYE SUBSTANCES AND THEIR SKIN SENSITISING PROPERTIES

COLIPA N°	Substance	Sensitising potency category	LLNA		GPMT		Buehler test		SCCP/SCCNFP opinion (doc. no.)
			EC3 value (%)	category	i.d. ind./incid.	category	t. ind./incid.	category	
	with 4-methylbenzenesulfonic acid (1:1)								
B75	Hydroxyethyl-2-nitro-p-toluidine	not classifiable	n.v.	not classifiable	-	-	-	-	SCCP/0924/05
C29	Acid Yellow 23	not classifiable	-	-	5/0	not classifiable	-	-	SCCNFP/0786/04
C40	Acid Blue 9	not classifiable	n.v.	not classifiable	-	-	-	-	SCCNFP/0787/04
C63	Acid Violet 43	not classifiable	n.v.	not classifiable	-	-	-	-	SCCP/0964/05
C67	Acid Blue 62	not classifiable	n.v.	not classifiable	-	-	-	-	SCCP/0878/05
C169	Lawsonia inermis (Henna)	not classifiable	-	-	-	-	50/0 f)	not classifiable	SCCP/0943/05
C174	Curry Red	not classifiable	n.v.	not classifiable	-	-	-	-	SCCNFP/0791/04
C175	Acid Red 18	not classifiable	n.v.	not classifiable	-	-	-	-	SCCNFP/0792/04
C177	Acid Red 52	not classifiable	-	-	5/0	not classifiable	-	-	SCCNFP/0803/04
C178	Acid Green 25	not classifiable	-	-	5/0 d,f)	not classifiable	-	-	SCCP/0879/05
A16	para-Aminophenol	j) i)	-	-	-	-	-	-	SCCP/0867/05
A80	Hydroxyethyl-p-phenylenediamine Sulfate	i)	-	-	-	-	-	-	SCCP/0666/03
A99	2,6-Dihydroxy-3,4-dimethylpyridine	j)	≤25 a); n.v.	?	-	-	-	-	SCCP/1034/06
B37	HC Blue N°2	j)	≤5 a); n.v.	?	-	-	-	-	SCCP/1035/06
C54	Acid Yellow 3	i)	-	-	-	-	-	-	SCCNFP/0789/04

Sensitisation potency category = based on the highest potency category from the tests with animal guideline methods (LLNA, GPMT, Buehler test)

EC3 value = EC3 values derived from LLNA dose-responses give the amount of chemical sensitiser that is required to elicit a three-fold increase in lymph node cell proliferative activity

i.d. ind./incid = intradermal induction concentration (%)/incidence of sensitisation (%)

t. ind./incid. = topical induction concentration (%)/incidence of sensitisation (%)

- = no data

n.v.=no value, stimulation index (SI) <3

not classifiable = the criteria for classification as R43, based on animal data, not fulfilled

a) = EC3 value was not calculated in the ref.

b) = The lowest test concentration was too high, an EC3 value could not be calculated

c) = The highest test concentration was too low, a stimulation index (SI) of ≥3 might have been achieved with higher concentration

d) = The induction concentration was too low

e) = The challenge concentration was too low

f) = Staining of the skin might have interfered with reading of test reactions

g) = The test was not acceptable

h) = Test vehicle may not be suitable

i) = Guinea pig test performed by non-guideline methods only

j) = Results indicate sensitisation potential

5. CONCLUSION

Contact allergy and allergic contact dermatitis caused by hair dyes is an important and increasing health problem to consumers and society, often causing acute and severe dermatitis on the face, scalp and neck.

Until now, the SCCP and the former SCCNFP opinions on substances, for which the dossiers submitted by industry have been assessed, have largely concerned the general toxicology of the substances, albeit there has been a statement regarding sensitising potential. Of the adopted opinions on 46 hair dye substances, 10 of these substances were categorised as extreme, 13 as strong and 4 as moderate skin sensitisers, all fulfilling the EU criteria for classification as a skin sensitiser (R43).

The SCCP wishes to state that hair dye substances which fulfil the criteria for classification as R43, may not be safe for consumers. This is particularly so for hair dye substances categorised as extreme and strong skin sensitisers.

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