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SCIENTIFIC COMMITTEE ON CONSUMER PRODUCTS

SCCP

Opinion on

**Review of the SCCNFP opinion on Hair Dye Strategy in the
light of additional information**

Adopted by the SCCP during the 8th plenary meeting
of 20 June 2006

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1. BACKGROUND

Commission services together with Member States agreed in April 2003 on a detailed programme of an overall strategy for the evaluation of hair dyes within the framework of the Cosmetics Directive 76/768/EEC. The strategy was published as *Information note on the use of ingredients in permanent and non-permanent hair dye formulations (dye precursors and direct dyes)* on

<http://europa.eu.int/comm/enterprise/cosmetics/doc/hairdyestrategyinternet.pdf>

This strategy has been decided following two opinions of the Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers (SCCNFP). In its opinion of June 2001 on "The Use of Permanent Hair Dyes and Bladder Cancer Risk" SCCNFP/484/01, the SCCNFP concluded that *the potential risk for the development of bladder cancer in past users of permanent hair dyes is of concern.*

The SCCNFP recommended that *the European Commission provides resources for the urgent review of the information, further epidemiological studies are performed to evaluate the possible association between bladder cancer and the use of permanent hair dyes in the EU and the European Commission takes further steps to control the use of hair dye chemicals since the potential risks of using this category of substances give cause for concern.*

In its opinion of December 2002 on "Assessment Strategies for Hair Dyes" SCCNFP/0553/02, the SCCNFP recommended an overall safety assessment strategy for hair dyes including the requirements for testing hair dye cosmetic ingredients for their potential genotoxicity and carcinogenicity. This safety assessment strategy is not restricted to the risk assessment of permanent hair dyes.

Therefore Commission services together with Member States agreed on a regulatory strategy to all hair dyes in use. The main element of the strategy is a tiered, modulated approach requiring industry to submit by certain deadlines files on hair dye substances to be evaluated by the SCCNFP. Thus the overall objective of this strategy is to regulate the use of these substances on the basis of scientific evaluation of files according to the most recent requirements of the Scientific Committee on Consumer Products (SCCP). Substances for which no file has been submitted for risk assessment by the SCCP will be treated on the highest priority basis whereas substances for which information is available will be regulated progressively.

As a first step, the strategy will ban all permanent and non-permanent hair dye substances for which no safety files had been submitted by the industry to SCCP until the end of September 2003. According to the hair dye strategy, dossiers for combinations of ingredients in permanent hair dye functions have to be submitted by industry at the latest December 2007 for the evaluation in SCCP.

In order to prepare the implementation of the first part of the strategy, COLIPA (European Cosmetics Toiletry and Perfumery Association) forwarded a list of substances in hair dyes for which no safety files are available. In its opinion on 23 April 2004 on "Hair dyes without files submitted" (SCCNFP/0807/04) SCCNFP concluded that those hair dye substances (permanent or non-permanent ones) identified on the COLIPA-list *'cannot be considered safe for hair dyeing*

purposes, unless they are regarded as such on the basis of an adequate safety dossier'. SCCNFP also pointed out that some of the substances listed may already be listed in the Cosmetics Directive, Annex III and Annex IV. If existing toxicological dossiers for these substances meet current requirements for safety evaluation, then they may be considered safe.

At the end of 2004, the European Commission received new publications on the possible link of occupation and hair colouring formulations to bladder cancer and non-Hodgkin's lymphoma as well as hair dye use and adult acute leukaemia. In its submission of 17 November 2004 DG Enterprise asked the Scientific Committee on Consumer Products (SCCP) whether this new information changes the overall assessment of the use of hair dyes and cancer risk as stated in the opinion of SCCNFP/0484/01 (updated in the opinion SCCNFP/0797/04).

In September 2004, the German Bundesinstitut für Risikobewertung (BfR) provided an opinion on hair dyes and on the hair dye strategy at European level: hair dyes on the Test bench: Their regulation at European level.' It concludes, in particular, that a differentiated handling of oxidative and non-oxidative hair dyes is justifiable. BfR recommends granting the extension of the deadline for submitting dossiers which are still outstanding for non-oxidative hair dyes.

2. TERMS OF REFERENCE

The SCCP is requested to review, and if appropriate, to amend the overall assessment of the use of hair dyes and cancer risk as stated in the opinion SCCNFP/0484/01, 0797/04 and 0807/04 on the basis of currently available scientific information and taking into account the attached opinion of the Bundesinstitut für Risikobewertung, "Hair dyes on the Test Bench: Their Regulation at European level" (14 September 2004), in particular with regard to non-permanent hair dyes.

3. INTRODUCTION

In its opinion of 17 December 2002 on Assessment Strategies for Hair Dyes, doc. n°SCCNFP/0553/02, the SCCNFP recommended an overall safety assessment strategy for hair dyes.

In particular, for the risk assessment of hair dye substances, the following must be submitted:

- The chemical specifications (purity and impurities) of the hair dye substances used, to generate the data, must be defined and be representative of those used in commercial products;
- According to the intended use, the dyes/dye-precursors must be tested alone and/or in combination with other substances to simulate the conditions of use;
- *In vitro*, and those necessary *in vivo*, studies required to identify the nature and the level of the possible hazards of hair dye substances;
- Data on genotoxicity – the studies must be consistent with internationally accepted guidelines (OECD, EU) and/or with modern testing strategies (doc. SCCNFP/0566/02);
- All available data on carcinogenicity;
- Deviations from the above must be justified.

This safety assessment strategy was not restricted to the risk assessment of permanent hair dye substances even if in the opinion the cause of concern was mainly focussed on the permanent dye substances (SCCNFP/0553/02):

“The European cosmetic industry uses a considerable number of permanent hair dyes and the safety of many of these has not yet been assessed by public authorities. The reasons for this include incomplete dossiers and non-conformation of experimental data to modern (current) methods of collection. European industry has submitted a list of those permanent hair dyes used at levels of > 2000 kg per year in Europe. This should be used as a priority list of substances requiring urgent assessment by the SCCNFP.”

In the strategy notes, to regulate the hair dye substances according to the SCCNFP requirements, the need for submission of dossiers by industry has been reinforced for:

- Individual dye precursors and dye substances for Permanent Hair Dye Formulations;
 - Individual dye precursors and dye substances for Non Permanent Hair Dye Formulations.
1. If no safety file has ever been submitted, the substance should be proposed for a ban. Deadline for submission: end of September 2003.
 2. Submission of safety files according to the new SCCNFP requirements (excluding data on combinations of ingredients). Deadline for submission: for all permanent and non-permanent hair dye, at the latest July 2005.
 3. 3rd step of the DG ENTR information note on the use of ingredients in permanent and non-permanent hair dye formulations (dye precursors and direct dye substances (updated March 2005): submission of dossiers by the industry for combinations of ingredients and evaluation by the SCCP (applicable only to dye precursors in permanent hair dye formulations). Deadline for submission: For combinations of dye precursors in permanent hair dye formulations, at the latest December 2007. *If no safety file is submitted according to the new SCCNFP requirements, substances should be proposed for a ban.*

In a recent updated opinion on “Use of permanent hair dyes and bladder cancer” (SCCNFP/0797/04), new data provided (Gago-Dominguez et al. 2003, Turesky et al. 2003, Czene et al. 2003) did not change the overall assessment of the use of permanent hair dyes and bladder cancer risk as stated in the opinion SCCNFP/0484/01 of 12 June 2001:

“Based on these findings, the Committee concluded that the potential risk for the development of bladder cancer in users of permanent hair dyes is of concern and requested a full quantitative list of all dye substances currently used in permanent hair dye formulations in the EU. Moreover, the committee recommended that the European Commission provides the resources for the urgent review of the information and performs further epidemiological studies to evaluate the possible association between bladder cancer and the use of permanent hair dyes in the EU.”

Very recently SCCP (20 September 2005-Opinion on personal use of hair dyes and cancer risk SCCP/0930/05) concluded that:

- a) Although the published data is conflicting, especially, when all types of hair dye formulations are considered, it is concluded that some studies indicate excess risks for acute leukaemia and chronic lymphoid leukaemia for users of hair dye formulations.
- b) It is concluded that there is an indication of excess risk of bladder cancer for women in USA using permanent hair dye formulations frequently and for long time.

4. OPINION

Safety assurance and with this, health protection of the consumer, can be applied only to those hair dye substances and complexes that have been subjected to the substances that the SCCNFP has listed in the document SCCNFP/0553/02. When a reviewed dossier contains incomplete or inadequate data, the SCCP may conclude that the information submitted is insufficient to allow an adequate risk assessment to be carried out. Accordingly, the SCCP considers that it is not possible to assess the safe use of the substance under consideration.

Hair dye substances are divided into three categories according to their colour fastness:

- a) temporary hair dye substances,
- b) semi-permanent hair dye substances,
- c) permanent hair dye substances.

Categories a) and b) are non-oxidative hair dye molecules (also known as direct or non-reactive hair dye molecules) and are used for transient colour changes.

- a) Colouring the hair by means of temporary hair dye substances takes place by depositing the higher molecular dye molecule on the surface of the hair, without it penetrating into the hair. The temporary colouring is removed by one to two shampooing.
- b) Semi-Permanent hair dye substances contain nitro compounds, e.g. small molecules that penetrate the cortex of the hair but that are on washing, gradually dissolved. The semi-permanent colouring fades after 6-8 shampooing.
- c) The group of permanent hair dye substances comprises oxidative hair dye molecules, the so-called oxidation hair dye molecules. The colouring is resistant to almost any number of shampooings and grows out over time. The colours are produced directly on and in the hair from precursors (developer and coupler) through chemical reaction in the presence of hydrogen peroxide as oxidising agent. This results in the hair being coloured right through and the colour is resistant to shampooing. Marketed permanent hair dye formulations contain often additionally other colorants (temporary or semi-permanent hair dye molecules).

The SCCP concern in relation to cancer comprises leukaemia and bladder cancer (SCCP/0930/05).

Leukaemia

The published data in relation to leukaemia are conflicting. Considering all types of hair dye formulations, an increased risk was found in 7 out of 12 case-control studies. Two European studies, one from Yugoslavia (Markovich-Denic et al., 1995) and one from Spain (Benavente et al., 2005) showed an increased risk of chronic lymphocytic leukaemia. Interestingly, in the latter

study the risk was only increased among those starting to use hair dye formulations before 1980. Three studies from USA were positive, particularly in relation to acute leukaemia (Markowitz et al., 1985; Cantor et al., 1988; Rauscher et al., 2004) and two studies on myelodysplastic syndrome from Japan showed an increased risk (Ido et al., 1996; Nagata et al., 1999).

Two cohort studies from the USA and four case-control studies concerning use of permanent hair dye formulations were evaluated. One of the cohort studies was borderline positive (all leukaemia) with a significantly positive trend for year of use ($p=0.04$) (Altekruse et al., 1999). One study from Spain (Benavente et al., 2005) was positive for chronic lymphocytic leukaemia, while one study from Italy was equivocal as it was overall negative (all leukaemia) while an increased risk was found among those using dark permanent products (Miligi et al., 1999). A recent study from America (acute leukaemia) (Rauscher et al., 2004) was positive.

Bladder cancer

Two cohort studies from the USA did not show any effect of permanent hair dye formulation use and bladder cancer. Four case-control studies have been evaluated. A recent study from Spain (Kogevinas et al., 2004) as well as an old small study from Canada were negative. Two recent studies from the USA were positive (Gago-Dominguez et al., 2001; Andrew et al., 2004). The study by Gago-Dominguez and co-workers is further supported by studies implicating arylamines contained in hair dye solution as the putative carcinogenic substances responsible for bladder cancer.

General considerations

The legislation of cosmetics and the regulation of ingredients in hair dye formulations in the EU and the USA differ. During the 1980's a number of putative carcinogenic hair dye substances were banned in the EU, but not in the USA. This may be one reason why no increased risk of bladder cancer was found in the study from Spain (Kogevinas et al., 2004) and that an increased risk of chronic lymphocytic leukaemia in Spain in relation to the use of hair dye formulations was only observed among those starting to use hair dye formulations before 1980 (Benavente et al., 2005). A second, less likely factor, may be a different contamination by impurities in the hair dye formulations used in the USA and the EU.

In 2001, the SCCNFP, after the publication of the Gago-Dominguez study, proposed a rigid testing strategy: dossiers for the authorization of all hair dye substances should have been submitted up to September 2003; hair dye substances for which dossiers were not submitted were to be banned. However, based on the above mentioned differences between the various types of hair dye formulations and based on the epidemiological evidence it seems reasonable to differentiate between the three different hair dye categories. In the case of temporary and semi-permanent hair dye formulations the consumer is exposed to substances which were subjected to toxicological testing. In contrast, for oxidative hair dye formulations, up to now, toxicological testing is performed only for developers and couplers. But in the reaction process transient intermediates as well as reaction products are formed on the scalp. The consumer is exposed to these. This problem was recently addressed in detail by an opinion of the SCCP (SCCP/0941/05).

5. CONCLUSION

Due to differences in technology of hair dye formulations, as well as in view of the epidemiological findings concerning various cancers, the SCCP supports differentiated approaches for the different types of hair dye substances involved. Priority should be given to the evaluation and regulation of oxidative hair dye substances.

The issue of sensitisation has not been addressed in this opinion.

6. MINORITY OPINION

Not applicable

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