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
12TH PLENARY MEETING

Brussels, 19 June 2007

MINUTES

1. WELCOME AND APOLOGIES

Dr. I.R. White welcomed all the participants. Apologies were received from Prof. G. Degen, Prof. R. Dubakiene, Dr. R. Grimalt, Prof. J. Krutmann and Prof. C. Lidén.

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 agenda was approved as proposed.

4. APPROVAL OF THE MINUTES OF THE 11TH PLENARY MEETING

The Minutes of the 11th plenary meeting were approved without changes.

5. INFORMATION FROM CHAIRMAN/MEMBERS

As follow-up to the presentation at the risk assessment days on 22 March 2007, Dr. White, as the chairman of the SCCP, will meet members of EP IMCO Committee on 12 September 2007.

6. EMERGING ISSUES

No issued 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. V. Rogiers presented a memorandum on the current status of alternative methods available for safety testing of cosmetics that was prepared by the working group.

Memorandum on Actual Status of Alternative Methods on the Use of Experimental Animals in the Safety Assessment of Cosmetic Ingredients in the European Union, doc. n° SCCP/1111/07

One of the mandates of the SCCP (former SCCNFP) defined by the Commission is to act as a resource of scientific expertise to the European Commission with regard to the development of alternative methods. In particular, the Commission has requested the former SCCNFP to assess the possibility to replace safety data obtained on the basis of animal tests with data obtained using alternative methods and to indicate those end-points for which no alternative methods are yet available (SCCNFP doc. n° 0177/99).

Therefore, the SCCP follows closely the scientific developments of alternative methods in order to identify the validated alternative methods that are applicable for the safety assessment of cosmetic ingredients and finished products.

As summarized in the 6th Revision of the "SCCP Notes of Guidance of the testing of cosmetic ingredients and their safety evaluation" (SCCP/1005/06), the specific hazard studies, necessary for human safety assessment of cosmetic ingredients, include acute toxicity, irritation and corrosivity (skin, eye), skin sensitisation, dermal absorption, repeated dose toxicity, mutagenicity/genotoxicity, carcinogenicity, reproductive toxicity, toxicokinetic studies, photo-induced toxicity and human data (if available).

The SCCP concluded that the actual status for alternative methods, suitable for cosmetic hazard testing is as follows:

- for 4 endpoints (skin corrosivity/irritation, dermal absorption, mutagenicity/genotoxicity, phototoxicity) validated replacement alternatives exist;
- for 2 endpoints (acute toxicity, skin sensitisation) validated reduction/refinement alternatives are available;
- for 5 endpoints (eye irritation, repeated dose toxicity, carcinogenicity, reproductive toxicity, toxicokinetics) no validated alternative methods are yet available.

Concern exists for the deadlines of March 2009 and 2013, which are unlikely to be met. Furthermore, the majority of alternative methods is not suitable for risk assessment of cosmetic ingredients, only for hazard identification.

The memorandum 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 21 March 2007.

Draft opinions were prepared on:

A79, 1,3-bis-(2,4-diaminophenoxy)propane, doc. n° SCCP/1098/07

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 1,3-Bis-(2,4-diaminophenoxy)propane and its tetra hydrochloride salt safe for use as non-oxidative hair dye formulations with a concentration of maximum 1.8 % (calculated as tetrahydrochloride salt, corresponding to 1.2 % of the free base) on the head taken into account the scientific data provided?*

2. *Does the SCCP consider 1,3-Bis-(2,4-diaminophenoxy)propane and its tetra hydro chloride salt safe for use as oxidative hair dye formulations with a final concentration 1.8 % on the head (calculated as tetrahydrochloride salt, corresponding to 1.2 % of the free base) taken into account the scientific data provided?*

3. *Does the SCCP recommend any restrictions with regard to the use of 1,3-Bis-(2,4-diaminophenoxy)propane and its tetrahydrochloride salt in oxidative or non-oxidative hair dye formulations (e.g. max conc. in the finish cosmetic product, dilution ratio with hydrogen peroxide etc.) beyond the existing allergenic warning?*

The SCCP concluded the use of 1,3-bis-(2,4-Diaminophenoxy)propane, and its tetrahydrochloride, itself as a oxidative and as a non-oxidative hair dye at a maximum concentration of 1.8 % (calculated as tetrahydrochloride salt, corresponding to 1.2 % of the free base) on the head does not pose a risk to the health of the consumer.

Beyond the existing allergenic warning, no further restrictions are deemed necessary.

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.

B31, HC Red n° 13, doc. n° SCCP/1075/07

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider HC Red No. 13 safe for use as a non-oxidative hair dye with an on-head concentration of maximum 2.5% taken into account the scientific data provided?*

2. *Does the SCCP consider HC Red n° 13 safe for use as an oxidative hair dye with an on-head concentration of maximum 1.25% taken into account the scientific data provided?*

3. *Does the SCCP recommend any further restrictions with regard to the use of HC Red n° 13 in any non-oxidative or oxidative hair dye formulations?*

The SCCP concluded that the information submitted is insufficient to allow a final risk assessment to be carried out.

Before any further consideration, an *in vitro* percutaneous absorption study should be performed following the relevant SCCNFP/SCCP opinions and in accordance with its Notes of Guidance.

HC Red n° 13 is a tertiary amine. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

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.

B70, 4-Nitrophenyl aminoethylurea, doc. n° SCCP/1037/06

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider 4-nitrophenyl aminoethylurea safe for use as a non-oxidative hair dye with an on-head concentration of maximum 0.5% taken into account the scientific data provided?*

2. *Does the SCCP consider 4-nitrophenyl aminoethylurea safe for use in oxidative hair dye formulations with an on-head concentration of maximum 0.25% taken into account the scientific data provided?*

3. *Does the SCCP recommend any further restrictions with regard to the use of 4-nitrophenyl aminoethylurea in any non-oxidative or oxidative hair dye formulations?*

The SCCP concluded that the information submitted is insufficient to allow a final risk assessment to be carried out. An additional mutagenicity / genotoxicity test should be performed following the relevant SCCNFP/SCCP opinions and in accordance with its Notes of Guidance in order to exclude its gene mutation potential.

4-Nitrophenyl aminoethylurea is a secondary amine. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

Its stability in the presence of hydrogen peroxide should be demonstrated.

The opinion was adopted.

B72, 2-Hydroxyethyl picramic acid, doc. n° SCCP/1058/06

The SCCP was asked to answer the following questions:

1. Does the Scientific Committee on Consumer Products (SCCP) consider 2-hydroxyethyl picramic acid safe for use as 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 2-hydroxyethyl picramic acid safe for use in oxidative hair dye formulations with an on-head concentration of maximum 1.5% taken into account the scientific data provided?

3. Does the SCCP recommend any further restrictions with regard to the use of 2-hydroxyethyl picramic acid in any non-oxidative or oxidative hair dye formulations?

The SCCP concluded that the information submitted is insufficient to allow a final risk assessment to be carried out. Before any further consideration, the possible genotoxic potential must be excluded.

2-Hydroxyethylpicramic acid is a secondary amine. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

2-Hydroxyethyl picramic acid is classified as toxic to reproduction category 3 (R62: possible risk of impaired fertility). The CMR classification was based on the assessment by BgVV (1993) on testes atrophy in the 450 mg/kg bw/day dose group of the 28-day study. However, more recent studies on reproduction toxicity do not support this classification.

The opinion was adopted.

B81, HC Yellow n°10, doc. n° SCCP/1080/07

The SCCP was asked to answer the following questions:

1. *Does the Scientific Committee on Consumer Products (SCCP) consider HC Yellow No. 10 safe for use in non-oxidative hair dye formulations with an on-head concentration of maximum 0.1 % in the finish product taken into account the scientific data provided?*

2. *Does the SCCP recommend any further restrictions with regard to the use of HC Yellow No. 10 in non-oxidative hair dye formulations (e.g. max conc. in the finish cosmetic product, dilution ratio with hydrogen peroxide, warning)?*

The SCCP concluded that the use of HC Yellow n° 10, itself as a semi-permanent hair dye at an on-head concentration of maximum 0.1%, does not pose a risk to the health of the consumer.

HC Yellow n° 10 is a secondary amine. It should not be used in combination with nitrosating substances. The nitrosamine content should be < 50 ppb.

The opinion was adopted.

Preliminary Opinion on Sensitivity to Hair Dyes – Consumer Self Testing, doc. n° SCCP/1104/07

The SCCP was asked to answer the following questions:

In the light of the data available,

1. Does the SCCP consider that there is a risk that:

- *Self-tests lead to false-negative results?*
- *Self-tests lead to induction of contact allergy?*

2. Does the SCCP consider that self-tests are beneficial for a specific population of hair dye users in order to detect existing sensitisations?

The SCCP concluded that:

When a hair dye product is applied to the skin for the purpose of providing an indication as to whether the individual consumer may or may not have contact allergy to hair dye chemicals(s), the product is being used for *in vivo* diagnostic purposes.

In response to the questions asked, the SCCP is of the opinion that:

- There is a risk that "self tests" with hair dye products and with separate kits lead to misleading and false-negative results, thus giving individuals who are allergic to hair dye substances the false impression that they are not allergic or not at risk of developing an allergic reaction by dyeing their hair.
- There is potential risk that "self tests" result in induction of skin sensitisation to hair dye substances.
- Self testing may offer protection to those individuals who perform the recommended test and develop a positive reaction. However, the proportion of hair dye chemical allergic individuals who do produce a positive reaction from this *in vivo* diagnostic test is unknown.

The SCCP wishes to point out that the use of hair dye products on the skin and for *in vivo* diagnostic purposes is not covered by the current Cosmetics Directive.

The preliminary opinion was approved for public consultation.

7.3. PRESERVATIVES AND FRAGRANCES

Report of the Co-ordinator

Dr. White said that no opinions had been prepared by the Working Party since the plenary meeting of 21 March.

7.4. UV FILTERS AND AD HOC SUBSTANCES

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

Kojic acid, doc. n° SCCP/1046/06

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider the use of kojic acid as a skin whitening or depigmenting agent in cosmetic products safe for the consumer?*

2. *Does the SCCP foresee any other concerns to the safe use of kojic acid?*

As a result of the discussion, the SCCP readdressed the draft opinion to the Working Party for further consideration.

Vitamin K1, doc. n° SCCP/1105/07

The SCCP was asked to answer the following questions:

1. *Does the SCCP consider that Vitamin K1 [and its oxide] are safe for the consumers when used in cosmetic products taken into account the provided data?*

2. *Does the SCCP recommend any restrictions to their safe use?*

As some points needed to be clarified, the SCCP decided to postpone the adoption of the opinion.

The opinion will be adopted by written procedure before the next plenary meeting of 2 October 2007.

Nano-materials in cosmetic products, doc. n° SCCP/1086/07

The SCCP was asked to answer the following questions:

1. *In view of the concerns recently raised about the use of nanomaterials in cosmetics the SCCP is requested to review and, if appropriate, to amend its notes of guidance for the testing of cosmetic ingredients and their safety evaluation as concern cosmetic ingredients*

in the form of nanomaterials, including nanoparticles and nanoliposomes, and in particular as regards skin absorption and resorption of these substances. In assessing this, regard should be made to differing skin conditions, different sizes of particles and to question whether mass unit is the appropriate basis for regulating the exposure to nanomaterials. Possible implications on animal testing of nanoparticles and nanoliposomes should be addressed.

2. *In the light of the findings under (1), does the SCCP consider it is necessary to review existing opinions on nano-sized TiO_2 and ZnO as cosmetic ingredients and if appropriate to identify which additional elements are required for the submission of a safety file?*

Responses to the questions in the Terms of Reference

Question 1

In the safety evaluation process, marketed nanomaterials should be used for material characterisation and hazard identification. Furthermore, distinction should be made between soluble and insoluble or slowly soluble nanomaterials. Nanoparticles which disintegrate into molecular species upon application have to be distinguished from insoluble particles. For the former, conventional risk assessment methodologies based on mass metrics may be adequate for cosmetics and their ingredients, whereas for the latter (e.g. TiO_2, ZnO, fullerenes, carbon nanotubes, and quantum dots) other metrics are needed. A complete characterisation of physico-chemical characteristics and properties is required for these nanomaterials. Particle size, particle number, shape and surface characteristics are considered essential additional metrics.

In traditional risk assessment, skin penetration studies are carried out using healthy or intact skin. Possible enhanced uptake in case of impaired skin is considered to be covered in the Margin of Safety (MoS) approach. In the case of assumed zero absorption, the MoS approach is possibly invalid. If there is any penetration into the vital layers of the skin there may be a transfer to the systemic circulation. It may be anticipated that any systemic absorption will be more likely in conditions of abnormal skin e.g. sunburned, atopic, eczematous, psoriatic skin. There is evidence that physical, in particular mechanical, and/or chemical action on the skin may have an effect on nanoparticle penetration.

At present, the *in vitro* diffusion cell chamber is the standard device for estimating percutaneous absorption. However, because mechanical factors may be important in potential penetration/absorption of nanoparticles, this standard model may not be ideal. Therefore, new methodologies to assess percutaneous penetration pathways are required.

There are large data gaps in risk assessment methodologies and with respect to nanoparticles in cosmetic products.

To evaluate possible pulmonary effects (and the linked systemic effects), simple *in vitro* systems exist, e.g. to study cytotoxicity, pro-inflammatory effects. However, these are not suitable for studying effects that reflect the complexicity of the lung. *In vitro* models for systemic and (sub-)chronic toxicity do not yet exist and need to be developed, in particular for biodistribution, translocation, accumulation and clearance studies. Therefore, *in vivo* studies on potentially toxic nanomaterials are still necessary.

Size dependence of the deposition probability of inhaled nanoparticles is reasonably understood in the respiratory tract of healthy subjects; however, for individuals with respiratory disorders predictions for nanoparticle deposition probability are very limited.

The biodistribution (toxicokinetics) of nanomaterials has not been studied in detail. Therefore, it is impossible to model, *in silico*, the distribution of nanomaterials. In particular, there is limited information on the role of physico-chemical parameters of nanoparticles determining their absorption and transport across barriers, e.g. skin, gut, lungs and eye, and their subsequent uptake in the systemic circulation, metabolism, potential accumulation in secondary target organs and excretion.

Although the requirements for testing the mutagenicity/genotoxicity of nanoparticles are similar to those of other particulate materials, the specific characteristics of nanoparticles may require further considerations. The genotoxic potential of nanoparticles could probably be assessed in mammalian cells *in vitro* provided that exposure of the nucleus at a relevant time for each assay is ascertained. The present validated *in vivo* genotoxicity tests, however, do not cover the expected target organs of nanoparticles (particularly the respiratory tract) and have not been validated with reference substances including nanomaterials of relevance for cosmetics.

All *in vivo* and *in vitro* risk assessment methods for nanomaterials are still under development. Although some validated in *vitro* methods do exist they have never been validated with nanoparticles as reference compounds. This implies that for safety assessment of cosmetic ingredients we are far from having validated *in vitro* methods for nanoparticles.

Whereas animal testing can be largely reduced for skin penetration studies, they are essential for translocation and accumulation studies as well as for chronic toxicity studies. Finally, the SCCP must emphasize that for the safety assessment of cosmetics, the 7th Amendment imposes animal testing and marketing bans, which will soon prohibit *in vivo* testing of cosmetics ingredients. Additionally, only validated *in vitro* methods may be used for risk assessment. At present, none of the methodologies mentioned above have been validated for nanomaterials. Each safety dossier would need to be evaluated on a case by case basis.

Question 2

A complete safety dossier on micronized and nanosized ZnO was requested by SCCNFP in its opinion on ZnO in 2003 (SCCNFP/0649/03). A submitted dossier is presently being evaluated by the SCCP.

The SCCNFP opinion from 2000 (SCCNFP/0005/98) is on micro-crystalline preparations of TiO_2 and preparations of coarse particles. However, since the opinion, a considerable amount of new scientific data on nanosized particles, including TiO_2 and concerns of possible carcinogenity[1] has become available. Therefore, the SCCP considers it necessary to review the safety of nanosized TiO_2 in the light of recent information. Also, a safety assessment of nanosized TiO_2, taking into account abnormal skin conditions and the possible impact of mechanical effects on skin penetration, needs to be undertaken.

[1] IARC has classified in 2007 all forms of titanium dioxide as a possible human carcinogen (group 2B substance) based on inadequate evidence in epidemiological studies and sufficient evidence for carcinogenicity in animal studies. The EU has not yet considered classification of titanium oxide.

The preliminary opinion was approved by the SCCP for public consultation.

8. NEXT PLENARY MEETING

The 13th plenary meeting of the SCCP will take place on 2 October 2007.

9. ANY OTHER BUSINESS

A presentation on future challenges for SANCO was given by C. Billaux, SANCO.2

- **Dates of WG meetings:**

10 July	Hair Dyes
17 July	ad hoc substances + Fragrances & Preservatives
31 August	Nano-substances in Cosmetics
11 September	ad hoc substances + Fragrances & Preservatives
18 September	Hair Dyes
25 September	Nano-substances in Cosmetics

Annex I: List of Participants.

Annex I

List of Participants

Members of the SCCP
Dr. C.M. CHAMBERS, Dr. B. JAZWIEC-KANYION, Prof. V. KAPOULAS, Prof. J.-P. MARTY, Prof. T. PLATZEK, Dr. S.C. 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)
Mr. T. DASKALEROS, Mrs. C. DEKINDT, Mrs. K. KILIAN, Mrs M. PUOLAMAA, Mr. A. VAN ELST

DG ENTR F3: Mrs. B. MENTRE, Mrs. A. ORLOFF