Scientific Committee on Cosmetic and Non-Food Products

Minutes of the 22nd Plenary Meeting

Brussels, 17 December 2002

Dr. Ian R. White, the chairman of the SCCNFP, welcomed all participants.

1. Adoption of the Agenda (doc. n° SCCNFP/0626/02)

The agenda was adopted.

2. The Commission strategy on Endocrine Disrupters

Dr. Claudia Roncancio, DG ENV, illustrated the Community Strategy for Endocrine Disrupters. The objectives are to identify the problem, its causes and consequences and to identify an appropriate policy action.

In the short term, the Commission intends to gather scientific evidence on certain substances for further evaluation of their role in endocrine disruption. In the long term, it might be necessary to adapt/amend the relevant EU legislation.

3. Declaration of interest

No Member declared any interest that could prevent her/him from participating in the discussion of any of the items on the agenda. Prof. Rogiers stated she considered it would be inappropriate for her to participate in the evaluation process of three colorants given to SCCNFP for consideration as she was acting as adviser to industry.

4. Approval of the minutes of the 21st plenary meeting of 17 September 2002, doc. n° SCCNFP/0608/02

The minutes were approved.

5. SCCNFP - Working Groups

5.1 Alternatives

Report of the Co-ordinator

In his report, Prof. Loprieno said that, since the previous plenary meeting of 17 September 2002, 2 meetings of the WG had taken place. The WG had focussed on the complete revision of the

Notes of Guidance. It is envisaged to present a first draft during the next plenary meeting of 18 March 2003 in order to inform the committee about the new format/style of the document.

Additionally, the WG has prepared a update of the document n° SCCNFP/0308/01 for possible adoption :

Basic Requirements for Toxicological Dossiers to be Evaluated by the SCCNFP update of 17 December 2002, doc. n° SCCNFP/0633/02

In view of recent developments, and in particular regarding papers recently adopted by the SCCNFP on the safety evaluation of hair dyes, it became necessary to adapt this paper and insert an additional point on hair dye ingredients.

The paper was adopted.

5.2 Detergents, Household & similar Products

Report of the Co-ordinator

Prof. Vives Rego said that one WG meeting had taken place since the previous plenary meeting of 17 December 2002 and during which the following issues had been discussed :

* Proposal for a Regulation of the EP and the Council on Detergents : although the systematic consultation of the SCCNFP on substances or preparations used in detergents that may pose a potential risk for the health of the consumer had been withdrawn from the initial proposal, the WG was pleased to learn that labelling provisions for preservatives and recognised fragrance allergens had been inserted. Nevertheless, a series of shortcomings regarding consumer health protection and information had been identified in the text. Dr. White, as the chairman of the SCCNFP, had brought these points to the attention of the Scientific Steering Committee (SSC) during its meeting on 7-8 November 2002.

* HERA documents : Prof. Vives Rego said that a further 7 documents (alkyl sulphates, fatty acids, LAS - alkylbenzene sulphonate, perboric acid, sodium carbonate, sodium percarbonate and Zeolite A) from the HERA-web site had been discussed.

It was decided to approve a SCCNFP statement on both items (see Annex 1).

5.3 Exposure & Risk Assessment

Report of the Co-ordinator

In his report, Prof. Schaefer said that, since the previous plenary meeting of 17 September 2002, no meetings of the WG had taken. However it was considered appropriate to summarise the main issues elaborated during the past two years :

- *Exposure in general* : industry has been requested to provide new and specific data on exposure of consumers to cosmetic products.

- *Cumulative exposure* : it is emphasised that other routes and sources of exposure to ingredients in addition to their use in cosmetics have to be taken into account, when calculating margins of safety.
- *Exposure areas* : areas of 700 cm² of scalp surface, of 1000 cm² of facial surface and of 18.000 cm² of whole body surface are defined.
- *Calculation of the Margins of Safety* : it is suggested to calculate the exposure to ingredients directly on the basis of µg/cm². Thereby the respective results of penetration studies is transformed into mg/kg exposure and related to NOAEL. Accordingly, an amended scheme for the calculation of margin of safety, and derived there from schemes for classes of cosmetic products may be necessary.
- *Exposure of children to sunscreens* : there is no scientifically sound reason to postulate an extra safety factor on top of the factor 100 for children above 1 year.
- *Exposure of infants* : industry has been requested to specify the exposure of the napkin zone to baby care products.
- *Vehicle effects on exposure and absorption* : the notion of prototype formulation for exposure and absorption studies in order to take vehicle effects into account.
- *Exposure to fragrances*.

Secondly, he mentioned issues to be addressed in the near future :

- Evaluation of industry expected response to recent requests;
- Exposure scenarios;
- Percutaneous Absorption studies in human volunteers;
- Quantitative Structure Absorption Calculations in risk estimation before first exposure to humans.

5.4 Hair Dyes & Colorants

Report of the Co-ordinator

In his report, Prof. Andersen said that besides the work of the special Task Force on Hair Dyes, set up to re-evaluate certain hair dyes currently listed in Annex III, part 2 of the cosmetics directive (26th adaptation), a series of meetings had been planned for early 2003 to evaluate the additional data received on 21 hair dye substances as well as 10 new dossiers. The hair dye issue will be a top priority for the coming year and the committee envisages to adopt opinions on all hair dyes for which safety data had been submitted. In this respect, the committee stressed again the need for a positive list of hair dyes and the need for samples of hair dyes to verify the quality of commercial hair dye formulations.

Assessment Strategies on Hair Dyes, doc. n° SCCNFP/0553/02

As a follow-up of its opinion on the use of permanent hair dyes and bladder cancer risk (doc. n° SCCNFP/0484/01 of 12 June 2001), the SCCNFP adopted during the 19th Plenary meeting of 27 February 2002 a discussion paper on “Assessment strategies on hair dyes”.

The main reasons to draft the paper were :

* a robust epidemiological investigation within Europe would take years to complete and there is a need for measures to be introduced to protect the European consumer in the interim;
* a considerable number of permanent hair dyes are used whose safety has not yet been assessed by public authorities.

Subsequently, the discussion paper was put on the web-page of the SCCNFP and interested parties were invited for their comments. Five comments were received from the scientific community, industry representatives and consumer organisations. None of these comments introduced elements to modify substantially the document.

The paper was adopted.

5.5 Inventory

Report of the Co-ordinator

In his report, Prof. Parra said that one meeting of the WG had taken place since the previous plenary meeting of 17 December 2002 and that no meetings of the WG are foreseen for the near future as the work on the 2nd update, to be initiated by DG ENTR, will not start before the 1st update has been adopted by the Standing Committee on Cosmetic Products.

Prof. Parra emphasised that in its opinion on the 1st update of the inventory of 28 June 2000 (doc. n° SCCNFP/0299/00), the SCCNFP highlighted a series of improvements to be made on the next update in order to achieve a more specific and transparent identification of the ingredients labelled on cosmetic products.

As a consultation with the SCCNFP is not mandatory, DG ENTR was invited to clarify its views regarding the tasks of the SCCNFP concerning the future updates of the inventory.

5.6 Preservatives & Fragrances

Report of the Co-ordinator

In his report, Prof. Kemper said that two WG meetings had taken place since the plenary meeting of 17 September 2002, during which the following opinions had been prepared:

Formaldehyde releasers

In the framework of its task to develop "methods of analysis necessary for checking the composition of cosmetic products" (Article 8), the Commission Working Party on Methods of Chemical Analysis of Cosmetic Products has observed that certain formaldehyde releasers in aqueous/polar solvents release some or all of their formaldehyde content : they do not remain as a single compound, nor do they remain 'intact' during chemical analysis. Four such formaldehyde releasers have been identified, namely imidazolidinyl urea, diazolidinyl urea, sodium hydroxymethyl glycinate and benzylhemiformal (entries 27, 46, 51 and 55 respectively in Annex VI, part 1 of the Directive). At present, it appears to be impossible to develop adequate methods to analyse these formaldehyde releasers in cosmetic products.

Determination of certain formaldehyde releasers in cosmetic products, doc. n° SCCNFP/0586/02

The SCCNFP was asked to answer the following questions :

* Does the SCCNFP consider possible to amend the above mentioned entries 27, 46, 51 and 55 so that the maximum authorised concentration could be expressed as a concentration of total formaldehyde without prejudicing the safety of cosmetic products?

* If so, can the SCCNFP propose maximum authorised concentrations of these preservatives,

expressed as total formaldehyde, in cosmetic products?

As a result, the SCCNFP did not recommend a general amendment of these entries, so that the maximum allowed concentration could be expressed as a concentration of total formaldehyde, because the following reasons:

- the safety profiles of the decomposition products of diazolidinyl urea and imidazolidinyl urea are unknown. However, it is considered that the decomposition products were present in the solutions of these substances used for the toxicological evaluation.

- due to the release of formaldehyde from imidazolidinyl urea and diazolidinyl urea, as well as due to the possible presence of formaldehyde from other ingredients, the level of free formaldehyde cannot be guaranteed during the lifetime of the product.

- in the absence of analytical methods for these four preservatives, consumer safety may be ascertained by adequately assessing the presence of formaldehyde in cosmetic products.

The opinion was adopted.

Clarification on the formaldehyde and para-formaldehyde entry in Directive 76/768/EEC on cosmetic products, doc. n° SCCNFP/0587/02

The SCCNFP was asked to answer the following questions :

* Does the SCCNFP consider possible to amend the above-mentioned entry 5 in a way so that the maximum authorised concentration could be expressed as a concentration of total formaldehyde without prejudicing the safety of cosmetic products?

* If so, can the SCCNFP propose maximum authorised concentration in cosmetic products as total formaldehyde?

As a result, the SCCNFP proposed not to amend entry 5 of Annex VI as stipulated in the mandate.

The opinion was adopted.

Opinion on P74 – 2,4-Dichlorobenzyl alcohol, doc. n° SCCNFP/0604/02

2,4-Dichlorobenzyl alcohol (DCBA) is regulated in the Cosmetic Directive 76/768/EEC, Annex VI, part 1, reference n° 22 and can therefore be used as a preservative up to a maximum authorised concentration of 0.15% in the finished cosmetic product. However, 2,4-Dichlorobenzyl alcohol bears the symbol (+) and can therefore be used in cosmetic products at higher concentrations, as long as it is not employed as a preservative.

The SCCNFP was asked to review the safety data submitted and to answer the question whether 2,4-Dichlorobenzyl alcohol can be safely used for non-preservative purposes in skin gels, creams, lotions, deodorants and shampoos up to a maximum concentration of 0.5 %.

As a result, the SCCNFP concluded that the information submitted is insufficient to allow an adequate risk assessment to be carried out. The genotoxicity/mutagenicity studies are inadequate (inadequate protocols) and do not allow a conclusive evaluation. Consequently, and before any further consideration, the following is required :

- adequate genotoxicity/mutagenicity data;
- the very high absorption rate (90%) should be further investigated using modern testing methods.
- cumulative exposure via other routes of application should be included in the assessment.

The final text will be redrafted and distributed through the secretariat for possible adoption following the written procedure.

Opinion on P81 – Zinc pyrithione, doc. n° SCCNFP/0482/01

Zinc pyrithione is regulated in the Cosmetic Directive 76/768/EEC, Annex VI, part 1, reference n° 8 and can therefore be used as a preservative up to a maximum authorised concentration of 0.5% in the rinse-off cosmetic products. However, zinc pyrithione is forbidden in oral hygiene products. Zinc pyrithione bears the symbol (+) and can therefore be used in cosmetic products at higher concentrations, as long as it is not employed as a preservative.

The SCNFP was asked to review the safety data submitted and to answer the question whether :

- zinc pyrithione can be safely used in rinse-off hair care products at a maximum authorised concentration of 1.0 % and in leave-on hair care products at a maximum authorised concentration of 0.1 %;
- zinc pyrithione can be safely used as a preservative in rinse-off hair care products at a maximum authorised concentration of 1.0 %.

As a result, the SCCNFP concluded that zinc pyrithione can be safely used under the above-mentioned conditions. The final text will be redrafted and distributed through the secretariat for possible adoption following the written procedure as soon as available.

5.7. UV Filters & Absorbers

Report of the Co-ordinator

In his report, Dr. Lina said that one meeting of the WG had taken place since the previous plenary meeting of 17 September 2002 during which the questions raised by the Danish EPA on S28, S38 and S60 were discussed:

- *Potential estrogenic effects* : the WG concluded that the issue has been answered in the Opinion on the Evaluation of Potentially Estrogenic Effects of UV-filters of 12.6.2001 (doc. n° SCCNFP/0483/01).

- *MOS for children*: also this issue has been answered in the Position Statement of 27.02.2002 on the Calculation of the Margin of Safety of Ingredients incorporated in Cosmetics which may be applied to the Skin of Children (doc. n° SCCNFP/0557/02).

- *Bio-accumulation*: the issue has been addressed by the WP 'Exposure & Risk Assessment' during its meeting of 16 April 2002.

The WP 'Exposure & Risk Assessment' concluded that : "The Danish EPA had made QSAR calculations which showed that 4-MBC (S60) may have intrinsic properties suggesting a potential for bio-accumulation. Therefore, they propose to further investigate 4-MBC regarding its concentration in the blood and its distribution in the organism.

It was said that (i) UV filters are normally large molecules with low dermal penetration, (ii) as the amount absorbed would be excreted in the urine, the blood levels will be low and consequently would require very sensitive analytical methods to be determined. Moreover, as all lipophilic substances might bio-accumulate and as there are no such previous cases in skin pharmacology, sub-chronic oral exposure could be take into account to demonstrate it.

Therefore, the WG concluded that the issue of bio-accumulation could not be reasonable answered unless the Danish EPA could clearly demonstrate it using QSAR."

- *Use of S28, S38 and S60 in 'products other than sunscreens'* : this issue has also been addressed by the WP 'Exposure & Risk Assessment' during its meeting of 16 April 2002.

The WP 'Exposure & Risk Assessment' concluded that : "The Danish EPA stated that the above mentioned UV filters are used in these products up to a concentration of 3.6%.

Unless proven otherwise, 100% of the ingredients in these products must be considered to be absorbed. In case of 4-MBC, this leads to an additional systemic exposure dose of 0.026 mg/kg bw. As lip protection is recommended in combination with sun screen products, the MOS changes from 110 to 96, which is not significant different."

It was decided that two specific working groups will be organised in January , in order to deal with "Fluoride compound in tooth paste for children" and the evaluation files P91 and S60, concerning endocrinology issues. The secretariat will coordinate the meeting dates between experts and chairmen of these groups.

6. Report of the Chairman

In his report, Dr. White said that a draft opinion on the use of Specified Risk Materials in cosmetics, and in particular on the derogation for tallow derivatives (entry n° 419 of Annex II to Directive 76/768/EEC on cosmetic products) had been drafted and that it was tabled for adoption.

Amendment to Entry n° 419 of Annex II to Directive 76/768/EEC on cosmetic products, doc. n° SCCNFP/0612/02

It appeared that the derogation for tallow derivatives, provided for in the current text of Entry n° 419, was possibly not in accordance with the opinions of the Scientific Steering Committee on :

- the safety of tallow obtained from ruminant slaughter by-products (opinion adopted on 28-29 June 2001);
- the risks of non-conventional transmissible agents, conventional infectious agents or other hazards such as toxic substances entering the human food or animal feed chains via raw material from fallen stock and dead animals (including also: ruminants, pigs, poultry, fish, wild/exotic/zoo animals, fur animals, cats, laboratory animals and fish) or via condemned materials of (opinion adopted on 24-25 June 1999 and re-edited during the meeting of 22-23 July 1999).

In order to clarify a possible discrepancy between the above mentioned opinions of the SSC and the opinion of the SCCNFP on the use of Specified Risk Materials in cosmetic products (entry 419 to Annex II), the SCCNFP was asked to answer the following questions :

* *Are exceptions made for tallow derivatives (provided that specific methods have been used to prepare them) scientifically consistent with the above mentioned scientific opinions of the SSC?*

* *If not, does the SCCNFP recommend that the list referred to in Regulation n° 999/2001 should be supplemented by the ingredients derived therefrom and no exceptions should be made regarding any of these ingredients?*

Based on the information presented in the above-mentioned opinions of the SSC, the SCCNPF concluded that the exceptions made for tallow derivatives in its latest opinion concerning the amendment to entry n° 419 of Annex II to Directive 76/768/EEC on cosmetic products (SCCNFP/0552/02 of 27 February 2002) are no longer scientifically consistent with the above mentioned scientific opinions of the SSC.

Consequently, the SCCNFP recommended that the list referred to in Regulation n° 999/2001 should be supplemented by the ingredients derived therefrom and that no exceptions should be made regarding tallow derivatives.

The opinion was adopted.

7. Any Other Business

* Prof. Schaefer announced the reasons for which he was no longer in a position to be a member of the SCCNFP. Dr. White expressed his deep regret and thanked Prof. Schaefer for this unique contributions to the scientific discussions of the SCCNFP. Prof. Schaefer offered his expertise whenever it is required by SCCNFP.

* *7th Amendment of Directive 76/768/EEC on cosmetic products* : Dr. Schumann said that, , the adoption is foreseen in January 2003, the final text it is not yet available.

* The secretariat explained that due to the high number of mandates and files pending to be evaluated, it is suggested that the SCCNFP members propose candidates to the secretariat in order to elaborate a list of experts for assistance on very specific issues, if the SCCNFP considers it.

* Following dates for 2003's meetings were agreed : 18 March, 24 and 25 June, 23 September and 11 and 12 November 2003

Attendance List

Present	:	Mr K.E. Andersen	Mr J.-P. Marty		
		Mr R. Anton	Mr J. Parra		
		Mrs C. Chambers	Mr T. Platzek		
		Mr A. Di Domenico	Mr S. Rastogi		
		Mr V. Kapoulas	Mrs V. Rogiers		
		Mr F. Kemper	Mr H. Schaefer		
		Mr C. Laurent	Mr T. Sanner		
		Mr B. Lina	Mr J. Vives Rego		
		Mr N. Loprieno	Mr I. R. White	(Chairman)	
Commission	:	Mrs S. Clarke	DG SANCO		
		Mrs L. D'Ambrosio	DG SANCO		
		Mrs R. Schumann	DG ENTR		
		Mr J. Serratosa	DG SANCO		
		Mr A. Van Elst	DG SANCO		

Annex 1

Report of the Co-ordinator of the WG "Detergents, Household and similar Products" 22nd plenary meeting of the SCCNFP of 17 December 2002

Two main activities have been undertaken by the WG "Detergents, Household and Similar Products" during the second part of the year :

A. Overview and comments on HERA detergent ingredients dossiers
B. Overview and comments on the proposal for a regulation of the EP and of the Council on detergents (COM(2002), 485 final)

A. Overview and comments on HERA detergents ingredients dossiers

HERA (Human and Environmental Risk Assessment) is a European industry project sponsored by the AISE and CEFIC (European Chemical Industry Council, http://www.heraproject.com) that has produced a number of documents on human and environmental effects of detergent ingredients. The WG has overviewed the following reports :

- Fatty acids (September 2002)
- Perboric acid (August 2002)
- Sodium percarbonate (August 2002)
- LAS - alkylbenzene sulphonate (July 2002)
- Alkyl sulfates (March 2002)
- Sodium carbonate (March 2002)
- Zeolite A (March 2002)

Since the WG has not received a specific mandate to provide a scientific opinion on these documents, formal reports have not been prepared but the following comments have been raised :

1. Exposure and Risk Assessment data are insufficient or unacceptable in some cases.

2. For optical brighteners, there is indication that at present no particular risk for consumers is seen, but it is considered that a final opinion only can be adopted when more exposure data are available.

3. The poisoning potential of detergents is discussed in HERA documents concerning LAS, sodium percarbonate and sodium carbonate. The HERA opinion refers to a report of the German Federal Institute for Health Protection of Consumers and Veterinary Medicine (BgVV, 1999) on products involved in poisoning cases. In these HERA documents it is stated that "*No fatal case of poisoning with detergents was reported in this report. Detergent products were not mentioned as dangerous products with a high incidence of poisoning"*.
A more recent report of the BgVV "Ärztliche Mitteilungen bei Vergiftungen, 2001", covering case reports from 1990 to 2001, lists 1770 cases relating to cleaning agents including detergents. From the data available it can be deduced that detergents per se do not play a major role in health

impairment while the accidental intake of cleaning agents may be critical in some groups of the population.

4. Industry has undertaken in-house risk assessments, and these are available on the internet; however, after general review of these documents, the WG feels that these risk assessments are based on inadequate studies (methods not according to modern standards, including OECD). Also evaluations undertaken by an independent agency are required. The genetic/mutagenic potential of all these chemicals or groups have not been adequately investigated by the recommended *in vitro* and *in vivo* methods as indicated by OECD and EC guidelines. Reports and summaries are inconclusive: they do not specify the methods applied and their limitation; they normally ignore or disregard positive data. Existing data are very old (from 1952) and do not conform to modern scientific requirements.

B. Overview and comments on the proposal for a regulation of the EP and of the Council on detergents (COM(2002), 485 final

In relation with the proposal for a regulation of the EP and of the Council on detergents (COM (2002), 485 final, the Working Group decided report to the SCCNFP plenary (and eventually to the SSC) the following comments :

* The objectives and scope (article 1, page 12) should be enlarged to include consumer health and safety protection. More consideration for human risk assessment needs to be given, since the present proposal is not adequate for consumer protection.

* Primary exposure and unintended exposure from use of detergents and household products as well as exposure of their residues need to be evaluated.

* Risk assessment with respect to human health aspect and safety has to be properly addressed in all scenarios and assessed case by case, and to be used in the risk assessment process;

* Allergic perfume ingredients are addressed in the current proposal through the SCCNFP opinions on fragrance allergens in cosmetic products. However, allergens other than those specified in this list need to be considered and adequately addressed. Complete labelling is required to fully protect/inform the consumer.

* The rule of Article 11[2] in the current proposal for labelling "in legible, visible and indelible characters on the packaging..." applies only to the name of the product, the trade name and address, and the datasheet address. However, the same rule is suggested for the information on labelling of contents and dosage information provided for in Annex VIII A, B and C (according to art. 11[3-5]. Furthermore, a restrictive sentence seems also necessary indicating that "labels shall not be misleading or give unrealistic information of the product and, in any case, indications such as 'low-risk', 'non-toxic', 'harmless', 'friendly to the environment', 'completely or 90% biodegradable', 'a cosmetic in your kitchen', 'with the softness of a baby' or similar indications or pictures", should avoided.

* A precautionary remark prompting consumers to use hand gloves in hand-washing application seems necessary since, according to literature data (ref. 1-14), epidemiological

studies have shown that household workers and cleaning personnel frequently have hand eczema that are etiologically linked to detergent exposure. Detergent preparations may also contain potent sensitisers leading to allergic contact dermatitis. In a Danish study based on cleaning agents for industrial and household use registered in the Danish Product Register Data Base (PROBAS), 49 contact allergens in 16 different product types within washing and cleaning agents were identified. The dermatologist is therefore regularly confronted with patients suffering from detergent-induced dermatitis. Most of the cases are irritant dermatitis that may be a risk factor for sensitisation and subsequent allergic contact dermatitis.

* Annex VIII-C would be more useful if was fully quantitative instead of semi-quantitative when to be used by health care professionals.

* Impurities of all ingredients need to be incorporated in the risk assessment process for both environmental and human health evaluation. (Note: Annex VIII-C defines that "Impurities shall not be considered to be ingredients").

* Musks and other bio-accumulative substances deserve attention from the environmental point of view.

* Potential endocrine disruptor properties of ingredients and impurities should include in these dossiers.

General comments on detergents and household products. (These general comments and the references cited below were taken from the Position Paper SCCNFP/0431/00 (Detergents -the dermatologist's view, P. Elsner)

Allergic contact dermatitis due to detergents : While irritant dermatitis is the most frequent dermatological condition induced by detergents, detergent preparations may also induce allergic contact dermatitis. While only few surface active agents are sensitizers (e.g. coconut diethanolamide), detergents may contain preservatives, antioxidants, fragrances, corrosion inhibitors, colouring agents, and other substances with a sensitizing potential. In a Danish study based on cleaning agents for industrial and household use registered in the Danish Product Register Data Base (PROBAS), 49 contact allergens in 16 different product types within washing and cleaning agents were identified.

Interaction of detergents with the skin : Surfactant penetration into the skin is associated with a swelling of the stratum corneum. Clinically, these changes correspond to the feeling of tightness. Non-ionic and hydrophobic binding of surfactants to the skin may occur.
Experimental sodium lauryl sulphate (SLS) exposure to human skin results in damage of the nucleated parts of the epidermis and alterations of the lower parts of the stratum corneum. The extrusion and transformation of lamellar body derived lipids into lamellar lipid bilayers are disturbed. However, the upper portions of stratum corneum display intact intercellular lipid layers contradicting the belief that surfactants damage the skin by delipidization.
Following SLS irritation, biological markers for epidermal growth and differentiation are unregulated. A rapid and strong induction of the cornified envelope precursor protein involucrin and of the epidermal fatty acid binding protein (E-FABP) was reported. Cellular proliferation in the basal layer is increased. Damage of keratinocytes is followed by release of mediators of inflammation with unspecific T-cell activation. IL-1 and TNF-alpha play a role as inflammatory

cytokines, IL-8 and IP-10 are known to act as chemotaxins, and IL-6, IL-7, IL-15, GM-CSF and TGF-alpha can promote growth. Other cytokines as IL-10, IL-12, and IL-18 are known to regulate humoral versus cellular immunity. In irritant reactions, the cytokines TNF-alpha, IL-6, IL-1ß, and IL-2 have been reported to be increased.

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