

OPINION OF THE SCIENTIFIC COMMITTEE ON COSMETIC PRODUCTS AND NON-FOOD
PRODUCTS INTENDED FOR CONSUMERS

CONCERNING

LINALOOL

adopted by the SCCNFP during the 26th plenary meeting
of 9 December 2003

1. Background

The SCCNFP adopted two opinions on fragrance allergy in consumers with an analysis of the need for appropriate consumer information and identification of consumer allergens (SCCNFP/0017/98, adopted during the 10th plenary meeting of 8 December 1999 and SCCNFP/0421/00, adopted during the 14th plenary meeting of 24 October 2000).

The SCCNFP identified 26 substances, used as fragrance ingredients, on which information should be provided to consumers about the known presence in cosmetic products. Because of the lack of dose/elicitation data for these substances, the SCCNFP had been unable to provide recommendations on levels above which the information to the consumers would be necessary. For practical risk management reasons, there is a need for threshold levels for the provision of information. For leave-on products, this should be 10 ppm in the finished cosmetic product and regarding rinse-off products, the SCCNFP would consider a working level ten times higher than that recommended for leave-on products to be reasonable (Memorandum on the SCCNFP opinion concerning fragrance allergy in consumers, adopted during the 16th plenary meeting of 13 March 2001, doc. n° SCCNFP/0450/01).

Council Directive 2003/15/EEC amended Directive 76/768/EEC by adding a list of the 26 fragrances mentioned by the SCCNFP in Annex III with the following limitation : “*The presence of the substances must be indicated in the list of ingredients referred to in Article 6.1.(g) when its concentration exceeds : 0.001% in leave-on products, 0.01% in rinse-off products*”. Linalool (CAS n° 78-70-6) is one of these 26 fragrances (Annex III, n° 84).

The European Commission received a letter from an association with a new technological and dermatological assessment of linalool and related esters when used as fragrance ingredients. This assessment was published in Food and Chemical Toxicology 41 (2003), authored by the Research Institute for Fragrance Materials (RIFM). In this assessment the RIFM Panel has determined that there are no safety concerns regarding linalool and related esters under the declared levels of use and exposure.

2. Request to the SCCNFP

The SCCNFP was asked to answer the following question :

Do the data provided justify that the opinions given by the SCCNFP on fragrance allergy in consumers do not apply to linalool?

3. Evaluation

About 1% of the normal population in Europe is sensitized to fragrance chemicals. The most commonly used fragrance chemicals are the terpenes obtained from natural essential oils. Of these terpenes, linalool from lavender oil is one of the most common fragrance chemicals in cosmetics, scented hygiene and skin care products and also in domestic and occupational products.

The re-evaluation of linalool is based on a new toxicological and dermatological assessment published in Food and Chemical Toxicology 41 (2003) authored by the Research Institute for

Fragrance Materials (RIFM) (1), and 3 other publications (2-4). Three more references have been detected and have been included in the evaluation.

Linalool is an unsaturated tertiary alcohol. It is a naturally occurring component together with linalyl esters in a variety of fruits, fruit peels, fruit juices, vegetables and spices as for example laurel, coriander seeds and clary sage. The annual worldwide use of linalool and linalyl acetate in fragrances exceeds 1000 metric tons.

For consideration of potential sensitization the exposure is calculated as a percent concentration used on the skin. Exposure to linalool used in fine fragrance products is reported as 4.3% based on the use of 20% of the fragrance mixture in the fine fragrance consumer product.

Experimental studies in laboratory animals combined with advanced chemical analyses have shown that linalool is easily oxidized, and that the content of linalool decreased to about 80% after oxidation for 10 weeks at standardized conditions. One of the major oxidation products was identified as 7-hydroperoxy-3,7-dimethyl-octa-1,5-diene-3-ol. In guinea pig sensitization studies a sample of oxidized linalool was a significant allergen sensitizing 8 of 15 test animals, whereas controls were negative. It was concluded that auto-oxidation is essential for the sensitizing potential of linalool. (3)

Bezard and co-workers have shown that linalyl hydroperoxide is a very strong sensitizer at the 1% level (5).

Further studies have documented the sensitizing capacity of linalool and derivatives. Basketter and co-workers found commercially available grade of linalool (97% purity) to be a weak sensitizer. When impurities were identified and removed the sensitizing capacity was reduced but not eliminated (6).

In the review presented at the RIFM 9th International Information Exchange, 2001 it is stated that in the presence of air, a number of common flavour and fragrance chemicals can form peroxides surprisingly fast. Antioxidants can in most cases minimise the oxidation. (4)

Recent clinical data support that linalool and its oxidation products are important contact allergens. Oxidized linalool and its hydroperoxide gave positive reactions in 1.8% of more than 1000 patients tested in a European multi-center study. A significant correlation to contact allergy to other fragrance materials was observed in all studies (7)

4. Response to the question

The SCCNFP is of the opinion that the submitted data, as well as other recent clinical data, do not support the request for linalool to be excluded from the opinion of the SCCNFP on fragrance allergens (doc. n° SCCNFP/0017/98 of 8 December 1999).

5. References

1. RIFM Toxicologic and dermatologic assessment of linalool and related esters when used as fragrance ingredients. *Fd. Chem Toxicol* 41: 919-1027, 2003
2. Skoeld m, Boerje A, Matura M, Karlberg A-T. Studies on the auto-oxidation and sensitizing capacity of the fragrance chemical linalool, identifying a linalool hydroperoxide. *Contact Dermatitis* 46:267-272, 2002
3. Skoeld M, Boerje A, Matura M, Karlberg A-T. Sensitization studies on the fragrance chemical linalool, with respect to autoxidation. Abstract. *Contact Dermatitis* 46: suppl 4 , 20, 2002

4. Bedoukian RH. Peroxide formation in aroma chemicals: the effect of chemical structure and antioxidants on product integrity. Proceedings RIFM 9th International Information Exchange, 20-39, 2001.
5. Bezard M, Karlberg A-T, Montelius J, Lepoittevin J-P. Skin sensitization to linalyl hydroperoxide: support for radical intermediates. Chem Res Toxicol 10: p87-993, 1997.
6. Basketter DA, Wright ZM, Colson NR, Patlewicz GY, Smith Pease CK. Investigation of the skin sensitizing activity of linalool. Contact Dermatitis 47: 161-164, 2002.
7. Karlberg A-T. Fragrance allergy: caused by oxidation of common fragrances: diagnosis and prevention. Abstract. 14th International Congress of Contact Dermatitis, Seoul, Korea, September 2003.