

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

OPINION

CONCERNING

METHYLDIBROMO GLUTARONITRILE

COLIPA n° P 77

Adopted by the SCCNFP on 23 April 2004
by means of the written procedure

1. Terms of Reference

1.1 Context of the question

Methyl dibromo glutaronitrile (1,2-Dibromo-2,4-dicyanobutane) is regulated in the Cosmetic Directive, Annex VI, part 1 n° 36 and can therefore be used as a preservative up to a maximum concentration of 0.1% in rinse-off products only (Directive 2003/83/EC of 24 September 2003, OJ L 238 of 25.9.2003, p. 23)

The European Commission received a letter from the chairman of the European Environmental & Contact Dermatitis Research Group (EECDRG) with data demonstrating the rising incidence of contact allergy to methyl dibromo glutaronitrile.

This letter was sent to the Health and Consumer Protection DG to pass on to the Scientific Committee on Cosmetic Products and Non-Food Products intended for consumer (SCCNFP).

The SCCNFP stated in its opinion concerning methyl dibromo glutaronitrile, COLIPA n° P77, adopted during the 20th plenary meeting of 4 June 2002 that:

- * the data show a clear rise in the incidence of contact allergy to methyl dibromo glutaronitrile throughout Europe and its use is a risk for the consumer.
- * the available data does show a dose response elicitation of allergic contact reactions to the preservative but provides no information on a 'safe level'.
- * until appropriate and adequate information is available to suggest a level of the preservative in leave-on products that poses an acceptable risk to the consumer (compared with the risk to the consumer from other preservatives), its use should be restricted to rinse-off products at the current maximum permitted level of 0.1%.

Recently, the Commission received further information on the safety of methyl dibromo glutaronitrile regarding possible effects of the substance on the thyroid gland.

1.2 Mandate to the SCCNFP (doc. n° ENTR 011678 of 21.10.2002)

The SCCNFP is requested to answer the following questions :

- * Is methyl dibromo glutaronitrile safe when used at the recently recommended maximum concentration in rinse-off products taken into account the data provided?
- * If not, does the SCCNFP consider that a lower concentration is safe for use in cosmetic products and do the data indicate such a concentration?
- * And/or does the SCCNFP recommend further restrictions than already recommended in its opinion adopted on 4 June 2002 with regard to the use of methyl dibromo glutaronitrile as a preservative in cosmetic products?

1.3 Statement on the toxicological evaluation

The SCCNFP is the scientific advisory body to the European Commission in matters of consumer protection with respect to cosmetics and non-food products intended for consumers. The Commission's general policy regarding research on animals supports the development of alternative methods to replace or to reduce animal testing when possible. In this context, the SCCNFP has a specific working group on alternatives to animal testing which, in co-operation with other Commission services such as ECVAM (European Centre for Validation of Alternative Methods), evaluates these methods.

The extent to which these validated methods are applicable to cosmetic products and its ingredients is a matter of the SCCNFP.

SCCNFP opinions include evaluations of experiments using laboratory animals; such tests are conducted in accordance with all legal provisions and preferably under chemical law regulations. Only in cases where no alternative method is available will such tests be evaluated and the resulting data accepted, in order to meet the fundamental requirements of the protection of consumer health.

2. Toxicological Evaluation and Characterisation

In response to the above-mentioned mandate, a re-evaluation of Methyl dibromo glutaronitrile was done, based on further information concerning the development of allergies received from the European Environmental & Contact Dermatitis Research Group (EECDRG) as well as on possible actions on the function of the thyroid gland mentioned in a letter of the EFTA delegate (Dr. H. J. Talberg, Norwegian Food Control Authority) to the Ad hoc Working Group Cosmetics (DG Enterprise).

In addition a "Final Report on the Safety Assessment of Methyl dibromo Glutaronitrile" (done by the Cosmetic Ingredient Review Expert Panel) published in the "Journal of the American College of Toxicology" (1996, 15, 140-165) as well as the "Registration Eligibility Decision Dibromodicyanobutane" List B, Case 2780 of the EPA/USA Office of Pesticide Program, Special Review and Preregistration Division, were at disposal. Moreover COLIPA - The European Cosmetic Toiletry and Perfumery Association - announced in the beginning of 2003 the formation of a special "Task Force on MDGN" dealing with questions regarding methyl dibromo glutaronitrile.

In the opinion SCCNFP/0585/02 on Methyl dibromo Glutaronitrile (MDGN) adopted on June 4, 2002, preferably dedicated to observations of an increase of allergic phenomena of MDGN, the Committee stated that recent epidemiological data have shown a clear rise in the incidence of contact allergies to MDGN throughout Europe. This indicates that the current use of MDGN-concentration and product types – is responsible for this observation. Finally the Committee came to the conclusion as there is at present no appropriate and adequate information available, the use of MDGN should be restricted to rinse-off cosmetic products at the current maximum permitted level of 0.1 % MDGN.

Besides the allergic phenomena the findings on thyroid alterations repeatedly occurred in several models but mostly after the administration of relative high doses/concentrations. Moreover most results on the thyroid gland were obtained in dogs, a species which has not been proven the best model of endocrine dysfunctions compared with man. In addition, also effects on the gastrointestinal tract, diarrhoea, emesis, as well as altered ovary weights in female rodents have been reported in the former dosing studies. Most of the respective investigations and their results have not been published in the open literature e.g. the papers by Wolffe (1980) and by Smith (1994) which especially could be of interest for a further evaluation. In the summary of another report increased pituitary weights in females and males and decreased testis weights in combination with altered thyroids are mentioned, as well as axonal degenerations in the brain and spinal cord. A TRH-test revealed apparently increased T4-/T3-response, suggestive of hypothyroidism. These statements are rather imprecisely transferred in the material under review. The effects of the compound on the pituitary, the ovary, the testis, have not been followed up in desirable detail or at least not presented in the dossier. As the compound also has moderate toxicity in fish (LC 50 of 1-4 ppm) some concern seems to be justified.

Moreover the compound seems not only to be distributed in cosmetic products, but can obviously also be found in a reasonable distribution and concentration in cleaning products and components of household products including wet toilet paper, a general evaluation needs to be required, especially as there are findings that food grade adhesives can contain MDGN up to a concentration of 0.005 % of dry weight fiber in the paper. Studies available indicate that MDGN is obviously absorbed to a high extent; nearly 50 % in 12 hours in the human and rat. Thus not

only dermal transfer pathways should be considered. In the light of the recent observations, the marked increase in use and distribution of the compound and the evidence for contact allergies and sensitization, a marked reduction in MDGN content, its distribution and application in general and in cosmetics seems mandatory, until further scientifically based information especially on its mechanism of action and morphological consequences, also on the endocrine system, are available.

3. Opinion

Methyl dibromo glutaronitrile causes contact allergies and has possibly effects on the endocrine system. Its mode of action is hitherto unknown. More scientifically based information is needed.

On the basis of the information attached to the above mentioned mandate, the SCCNFP is of the opinion that there is no scientific basis to change its opinion concerning methyl dibromo glutaronitrile, adopted during the 20th plenary meeting of 4 June 2002 (doc. n° SCCNFP/0585/02).

4. References

1. Final Report on the Safety Assessment of Methyl dibromo Glutaronitrile. The Cosmetic Ingredient Review Expert Panel. Journal of the American College of Toxicology, 1996, 15(2): 140-165
2. Registration Eligibility Decision Dibromodicyanobutane” List B, Case 2780 of the EPA/USA Office of Pesticide Program, Special Review and Preregistration Division
3. Letter of 3 September 2002 to the Chair of the EU Commission’s WP on Cosmetic Products from the EFTA delegate Hans Jorgen Talberg, Norwegian Food Control Authority