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## Contact allergy to the preservative methyldibromoglutaronitrile

### Summary

In recent years the cosmetic preservative methyldibromoglutaronitrile (MDBGN) has gained notice due to a significant increase in the frequency of contact allergy to the chemical in Europe. A 10-year analysis, involving 16 dermatological clinics in 11 European countries, revealed a rise in the average frequency of sensitivity to MDBGN from 0.7 in 1991 to 3.5 in 2000 in consecutive eczema patients. These observations promote MDBGN to an important contact allergen in Europe.

The aim of this project was to characterize different aspects of the allergic response to MDBGN in previously sensitized individuals. During 3 clinical elicitation studies, sensitized subjects were exposed to the preservative in experimental use tests designed to resemble the actual use-situation of cosmetic products among consumers. Aspects examined were: the allergic response to MDBGN in a rinse-off product, the implication of application frequency, and the significance of previous exposure.

Some types of rinse-off products, e.g. liquid soaps, are potentially used many times a day and may thus carry a similar risk of causing contact allergic contact dermatitis as leave-on products (moisturizers, lotions etc.) used only once or a few times a day. The EU Commission service has requested a revision of the use-level of MDBGN in leave-on products, while the use of MDBGN in rinse-off products is unchanged. The first experiment investigated the allergic response elicited in pre-sensitized individuals from exposure to a rinse-off product preserved with the maximum permitted level of MDBGN. 19 contact-allergic individuals participated in a double-blind, randomized repeated open application test (ROAT) using two coded liquid soaps with and without MDBGN. 7/19 subjects (37%) developed allergic contact dermatitis from the MDBGN-containing soap. The experiment showed that the exposure to a rinse-off product containing the maximum permitted level of MDBGN easily can elicit allergic contact dermatitis in pre-sensitized individuals and indicates that the permitted level of MDBGN in rinse-off products may be too high. It is recommended that the currently allowed level of MDBGN in rinse-off products is re-evaluated.

The second experiment examined whether one high-dose exposure a day of MDBGN is more or less potent than several low-dose exposures with regard to elicitation of allergic contact dermatitis in pre-sensitized individuals. This knowledge may be useful in the risk assessment and regulation of cosmetic ingredients in products potentially used several times a day. MDBGN-sensitized individuals were exposed to MDBGN in a double-blind, randomized manner both with a single high-dose application a day and with 4 low-dose applications a day. The daily high-dose and multiple low-dose exposures had approximately equal capabilities of eliciting allergic contact dermatitis.

According to this study, particular care must be taken in the risk assessment of products containing MDBGN that may be applied to the skin several times in one day. Examples of this could be occupationally used products, like soaps and hand-care products.

The aim of the third trial was to investigate whether skin with previous dermatitis elicited by MDBGN showed an augmented response when re-exposed to the allergen. Challenge was performed both by patch testing and in a use test with an MDBGN-containing soap. Areas of allergic contact dermatitis were elicited on the back and on the arms of 17 MDBGN-sensitized individuals. After one month, the previously eczematous areas were challenged with MDBGN. On the back of the subjects, the test sites were patch tested with a serial dilution of MDBGN and a use test was performed on the arms with an MDBGN-containing soap. A statistically significant augmented patch test response was seen on the back areas with previous dermatitis. 9 patients developed dermatitis on the arms from exposure to the MDBGN-containing soap in the use test. Of these, 8 had an augmented response on the areas with prior allergic contact dermatitis. Even though allergic contact dermatitis appears healed, an increased reactivity to exposure from the allergen that elicited the pre-existing dermatitis is present.

In summary it was concluded that 1) MDBGN in rinse-off products can elicit allergic contact dermatitis in sensitized individuals, 2) multiple daily exposures to MDBGN appear to accumulate, and 3) skin areas with previous allergic contact dermatitis from MDBGN are hyperreactive to re-exposure both by patch testing and in a use test even though the skin appears clinically healed.