Note Regarding the Safety Assessment of Chlorhexidine, Chlorhexidine Diacetate, Chlorhexidine Digluconate, and Chlorhexidine Dihydrochloride[1]

This note alerts readers to new information regarding the safety of Chlorhexidine, Chlorhexidine Diacetate, Chlorhexidine Digluconate, and Chlorhexidine Dihydrochloride.

The Cosmetic Ingredient Review (CIR) Expert Panel earlier published a safety assessment of the use of these ingredients in cosmetic formulations (Andersen 1993). In this report the Panel reached the following conclusion: "*On the basis of the data presented in this report, the CIR Expert Panel concludes that Chlorhexidine and its salts are safe for use in cosmetic products at concentrations up to: 0.14% calculated as Chlorhexidine free base; 0.19% as Chlorhexidine Diacetate; 0.20% as Chlorhexidine Digluconate; and 0.16% as Chlorhexidine Dihydrochloride.*"

Recently, the U.S. Food and Drug Administration (FDA) issued a public health notice regarding potential hypersensitivity reactions to chlorhexidine-impregnated medical devices (FDA 1998). This notice informed health care professionals about the potential for serious hypersensitivity reactions that may not be well known to device users, while acknowledging that the full extent of the problem is not clear.

The CIR Expert Panel had noted in its earlier safety assessment that sensitization was a concern. There were case reports of patients treated with a Chlorhexidine disinfectant that suggested anaphalactic shock reactions. After careful review of those data, however, the Panel concluded that only one clinical report in patients treated with a Chlorhexidine disinfectant could possibly be considered an anaphalactic shock reaction.

Based in part on clinical test data of mouthwashes containing 0.2% Chlorhexidine Digluconate which showed no sensitization, the conclusion (*in italics above*) was reached that a concentration limitation would be sufficient to ensure safety (Andersen 1993).

The CIR Expert Panel reviewed the evidence of hypersensitivity reactions in patients exposed to chlorhexidine-impregnated medical devices presented by FDA in its public health notice (FDA 1998). Many of these reports were not new and were considered by the CIR Expert Panel in its safety assessment. These reactions reported by FDA occurred to topically applied chlorhexidine, chlorhexidine gels/lubricants used in urological procedures, to central venous catheters impregnated with chlorhexidine, and to other chlorhexidine containing devices. Those case reports that are new are similar to those previously considered by the CIR Expert Panel and are indicative of an IgE-mediated allergic reaction.

Although these data did not suggest to the CIR Expert Panel a need to change the conclusion regarding the safe use of chlorhexidine as a preservative in cosmetic formulations, reports of IgE-mediated allergic reactions are considered serious. Working with FDA, the Panel will monitor such reports to be certain that no increase in frequency is occurring. Meanwhile the Panel reiterates to the cosmetic industry the critical importance of limiting the use of these ingredients to the concentrations specified in the CIR safety assessment as follows:

> Chlorhexidine and its salts are safe for use in cosmetic products at concentrations up to: 0.14% calculated as Chlorhexidine free base; 0.19% as Chlorhexidine Diacetate; 0.20% as Chlorhexidine Digluconate; and 0.16% as Chlorhexidine Dihydrochloride.

REFERENCES

Andersen, F. A., ed. 1993. Final report on the safety assessment of Chlorhexidine/Chlorhexidine Diacetate/Chlorhexidine Digluconate/Chlorhexidine Dihydrochloride. *J. Am. Coll. Toxicol.* 12:201–223.

Food and Drug Administration (FDA). 1998. *FDA public health notice: Potential hypersensitivity reactions to chlorhexidine-impregnated medical devices.* Rockville, MD: FDA. http://www.fda.gov/cdrh/chlorhex.html (4 pages).

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