INTRODUCTION
Traditional preservation systems currently used in cosmetic and skin care products are safe and effective. New ingredients with similar efficacy are continually being introduced to fulfill this function. A new preservative system containing 1,2-hexanediol and caprylyl glycol (Symdiol® 68) provides one such alternative allowing reduction in the use of parabens and formaldehyde releasing preservatives. This clear colorless liquid is effective in a wide variety of vehicles with broad spectrum antimicrobial properties.

OBJECTIVE
To study the potential for delayed Type IV dermal sensitivity and irritation of a preservative system containing 1,2-hexanediol and caprylyl glycol.

METHODOLOGY
A 200 subject Repeat Insult Patch Test (RIPT) was performed (1). Subjects with any visible skin disease, active psoriasis or eczema, known sensitivity to cosmetics, skin care products or topical drugs, pregnant or nursing or on medication with any medical condition which might interfere with the study results, were excluded. 20 uL of a 15% mixture of 1,2-hexanediol and caprylyl glycol (equal parts of the two ingredients) in carbomer gel was placed under a series of 9 continuous occlusive induction patches, each 48 hours in duration. Three induction patches were applied each week, for a total of 3 weeks. Following a 10-day rest period during which no patches were applied, a single challenge application using the same mixture was applied and left on for 48 hours and read at 48 and 72 hours post-application.

Dermatologic grading was done according to the following scale (2):
+ - definite erythema without edema
++ - definite erythema with edema
+++ – definite erythema, edema and vesiculation
D – damage to the epidermis: oozing, crusting and/or superficial erosions

A cosmetic formulation containing this same preservation system (gel vehicle) at an actual use concentration (0.5%) was tested by the same RIPT protocol.

RESULTS
232 subjects were enrolled in the study. 205 subjects completed the study. 163 were female and 42 were male ranging in age from 18 to 70. 27 subjects discontinued for personal reasons. One subject experienced a D reaction at the seventh induction patch. This same subject showed no reaction on challenge. Otherwise no reactions were seen during the induction or challenge phases.

The single subject with a D reaction subsequently underwent a Repeat Open Application Test consisting of four daily applications of the test material to the antecubital fossa and five evaluations. On Day One 20 uL of the 15% test mixture was applied over approximately a 2 cm X 2 cm area with no immediate reaction after that day or on the subsequent four days when the same material was reapplied.

An additional 248 subjects were enrolled in a separate RIPT that evaluated the cosmetic formulation containing this same preservation system. 224 subjects completed the study. 176 were female and 48 were male ranging in age from 19 to 70. No delayed Type IV dermal sensitivity or irritation reactions were observed.

DISCUSSION
The Repeat Insult Patch Test is considered the most reliable study for predicting the likelihood of an ingredient or a product producing contact hypersensitivity in naive human subjects (2). The protocol followed here with continuous 48 hour patches as opposed to 24 hour applications is arguably a more rigorous version of this study also simulating a cumulative irritation study (3). The use of a 15% mixture 1,2-hexanediol and caprylyl glycol represents twenty to thirty fold increase from actual use concentrations. Despite this exaggerated level no instances of sensitization was observed. Irritation was only seen in one subject. This subject’s reaction upon 7th induction was not reproduced during challenge which is indicative of irritation as a function of exaggerated contact with occlusive patches and not sensitization. This conclusion was corroborated by a subsequent Repeat Open Application Test.

A second study using the same protocol with an actual cosmetic product containing these preservatives showed no instances of irritation or sensitization.

CONCLUSION
A new preservative system utilizing 1,2-hexanediol and caprylyl glycol did not induce delayed Type IV dermal sensitivity or significant irritation in human subjects and can be considered safe for use in cosmetic products.

REFERENCES

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