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G-66 Guerbet Ester Toxicology Studies

CTFA / INCI Name: Trioctyldodecyl Citrate

Acute Oral Toxicity

The acute oral toxicity of G-66 Guerbet Ester was studied in rats according to FHSLA, 16 CF 1500.3. Five male and five female rats were administered a single dose of 5,000 mg/kg via gavage. The animals were housed individually and observed for mortality and clinical signs of toxicity for 14 days following exposure. No evidence of toxicity was observed. The acute oral LD_{50} was determined to be greater than 5,000 mg/kg.

Eye Irritation

The potential for G-66 Guerbet Ester to cause eye irritation was evaluated according to FHSLA, 16 CFR 1500.42. A dose of 0.1 ml of the test material was administered to eyes of six rabbits. The eyes were evaluated according to the method of Draize et al.[1] The Draize scores were then classified according to the method of Kay and Calandra.[2] The eyes were evaluated at 24, 48, and 72 hours following exposure. The Maximum Mean Total Score was determined to be 0.00. Based on these results the test material was considered to be non-irritating.

Skin Irritation

The skin irritation potential of G-66 Guerbet Ester was evaluated according to FHSLA, 16 CFR 1500.41. A dose of 0.5 ml of the test material was applied to the intact and abraded skin of six rabbits and then covered by occlusive patches. The skin was evaluated at 24 and 72 hours. The Primary Irritation Index was determined to be 0.00. Based on these results the test material was not considered to be a primary skin irritant.

Skin Sensitization

The irritation and sensitization potential of the test material was evaluated using the human repeat insult patch test. The test material (150 µl) was applied to a 2 cm x 2 cm absorbent pad centered on the adhesive-coated surface of a 4 cm x 4 cm water-impermeable plastic film that then was positioned on the skin of 107 human volunteers.[3] For the induction phase a series of 12 applications, four consecutive applications per week for three weeks, was conducted with each panelist at the designated site. The patches were removed and the contact sites were examined 24 hours after each application. Following a two week rest period, the challenge phase was conducted using 4 applications of the test material and evaluations on a naive site of each volunteer. A final evaluation of the sites was provided the following week. No skin irritation or sensitization responses were observed

[1] Draize et al., (1944) J. Pharmacol. Exp. Ther. 83:377-390.
[2] Kay and Calandra, (1962) J. Soc. Cos. Chem. 13:281-289.

[3] 107 volunteers participated in the induction phase; 105 completed the challenge phase

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with the test material during the course of the study. The investigators concluded that the results do not contraindicate skin contact with the test material under equal or less stringent conditions.

The skin sensitization potential of a number of samples of the test material was evaluated in the mouse using the Local Lymph Node Assay based on the guidelines described in OECD, Section 4, Health Effects, No. 429 , Paris Cedex, April, 2002, EC, Council Directive 67/548/EEC, Annex IV C, B.42 (Draft), June 2001 and US EPA , OPPTS 870.2600, March 2003. Groups of five mice were treated with the test material a concentrations of 0%, 10%, 50%, and 100% w/v in acetone/olive oil (4:1 v/v) (25 µl/ear) by daily application to the dorsal surface of each ear for three consecutive days. Five days following the first topical application, all mice were injected with 0.25 ml of phosphate buffered saline containing 3H-methyl thymidine via tail vein giving a total dose of 20 µCi to each mouse. A single cell suspension of pooled lymph node cells was prepared by mechanical disaggregation through stainless steel gauze (125µm diameter). The cells were washed and centrifuged, precipitated, and re-centrifuged at 4^{o} C, and then were measured for ^{3}HTdr incorporation. Alpha-hexylcinnamic aldehyde in acetone/olive oil (4:1 v/v) as 5%, 10%, and 25% solutions were used as the positive control. Untreated controls also were included.

Slight erythema was noted in a few animals in the two highest dose groups. The majority of lymph nodes were normal; enlarged nodes were observed in one animal in the vehicle control and the 50% group and in two animals in the 100% group. The stimulation index (SI) for the test substance concentrations tested were found to range from 1.1 to 3.1. Because the SI values for several of the test substance concentrations were above the criteria for a positive response (test/control ratio > 3), the test substance was determined to cause a sensitization response under the conditions of this test. The EC3 value was calculated to be 95.8%. Under the current proposed classification scheme the neat test material may be considered a mild sensitizer. Furthermore, based on these results it was concluded that the neat test material should be labeled as: may cause sensitization by skin contact (R43).