



FRAGRANCE MATERIALS ASSOCIATION OF THE UNITED STATES

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Via Federal Express

MR 296701

June 20, 2006

Contains No CBI

TSCA Confidential Business Information Center (7407M)

EPA East Room 6428

Attn: TSCA Section 8(e) Coordinator

U.S. Environmental Protection Agency

1200 Pennsylvania Avenue., N.W.

Washington, D.C. 20460-0001

Telephone - 202-564-8940

CONTAINS NO CBI

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OPPT/CBIC

RE: Oral (Gavage) One Generation Reproduction Study 3 and 4-(4-Hydroxy-4-methylpentyl)-3-cyclohexene-1-carboxaldehyde (CAS No. 31906-04-4) in rats

Dear TSCA 8(e) Coordinator:

On behalf of its members, the Fragrance Materials Association of the United States (FMA) is reporting test results from an oral (gavage) one generation reproduction study of 3 and 4-(4-Hydroxy-4-methylpentyl)-3-cyclohexene-1-carboxaldehyde in rats. The CAS number for this substance is 31906-04-4.

FMA is submitting information on this study pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA). This information was received through a draft final report from the contract laboratory that performed the study, SafePharm Laboratories (Hereford, England). Two FMA members companies, Takasago Inc. and International Flavors & Fragrances Inc., sponsored this study.

This study does not involve effects in humans. This notification does not contain confidential business information.

Study Summary

The material or the vehicle, Arachis oil BP, were administered orally (via gavage) at dosages of 0 (vehicle), 25, 100, and 500 mg/kg body weight/day to 24 Sprague-Dawley Crl:CD® (SD) IGS BR rats per sex per group. The dose volume was 4 ml/kg body weight. After 10 weeks of treatment for males and two weeks of treatment for females, paring of animals within each dose group was undertaken. All surviving males were sacrificed following evidence of a successful mating phase. Pregnant females were allowed to give birth and maintain their offspring until Day 21 post partum at which time all surviving females and offspring were sacrificed. Females continued to be dosed during the gestation and lactation phases.

Under the conditions of this study, there were no treatment related effects on female estrous cycles, or on mating or fertility or intergroup differences in gestation or parturition indices.



At the high dose the live birth index was significantly lower than control animals with litter size continuing to be statistically lower than control animals throughout lactation. In this treatment group, body weight gain was lower than control animals for the first week of age and again from Day 14 to Day 21 and litter weight was notably lower through out lactation. A delay in the onset and completion of pinna unfolding was also evident in offspring together with a reduction in the number of offspring passing surface righting, air righting, pupil reflex and startle reflex assessments. A total of eight 500 mg/kg body weight/day litters had not fully completed eye opening by weaning. This dose was also severely toxic to the dams resulting in maternal deaths associated with dystocia and evidence of maternal stress.

Skin sloughing was detected in offspring during the first week of lactation (beginning on Day 3 post partum) in the groups receiving 500 and 100 mg/kg body weight/day. This was more pronounced in the high dose group. There were multiple ridges along the tail in the 500 and 100 mg/kg body weight/day litters. Swollen ears became apparent in the 500 and 100 mg/kg body weight/day litters together with premature opening of eyes and sparse fur coverage in the high dose litters. No effects were detected at a dose of 25 mg/kg body weight/day.

Acanthosis and hyperkeratosis were seen in relation to treatment for the skin of male and female F₁ generation animals treated with 500 and 100 mg/kg body weight/day.

The NOEL for adult toxicity was therefore considered to be 100 mg/kg body weight/day and the NOAEL for reproductive and developmental toxicity was considered to be 25 mg/kg body weight/day.

Please contact me if you have any questions or require additional information. My telephone number is 202-293-5800.

Sincerely,



Glenn Roberts
Executive Director