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26 July 2012

US EPA Office of Pollution Prevention and Toxics
EPA East Building - Room 6428 - Attn: Section 8(e)
1201 Constitution Avenue, NW
Washington, DC 20004-3302

United Initiators, Inc.
555 Garden Street
Elyria, Ohio 44035
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Return Receipt Requested



SUBJECT: TSCA 8(e) Notice

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Dear TSCA Section 8(e) Coordinator:

On behalf of the study sponsor named below I am submitting results for OECD 422 test (Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test) with tert-Butyl Peroxyneodecanoate (CAS# 26748-41-4, our product notation TBPND). The study sponsor is United Initiators GmbH & Co. KG.

Study details:

Reference: report study 552.439.3245

Performed by: TOXI-COOP ZRT, Hungary

Study Summary:

The purpose of this Combined Repeated Dose Toxicity Study with the Reproduction/Developmental toxicity screening test was to provide initial information concerning the toxic potential of TBPND and on its possible effects on male and female reproductive performance such as gonadal function, mating behaviour, conception, pregnancy, parturition as well as on development of the F1 offspring from conception to day 4 post-partum associated with oral administration to rats at repeated doses.

Four groups of Hsd.Brl.Han:Wist rats (n=12/sex/group) were administered orally (by gavage) once a day at 0 (vehicle only), 60, 200 and 600 mg/kg bw/day at concentrations of 30, 100 and 300 mg/mL corresponding to 2 mL/kg bw dose volume.

Results:

There was no test item related mortality at any dose level (600, 200 and 60 mg/kg bw/day).

Test item related salivation appeared in male and female animals administered with 600, 200 and 60 mg/kg bw/day groups in all with a dose related degree, onset and incidence. No toxic signs related to the test item were found at the detailed weekly and terminal functional observations. The behavior and physical condition of animals were normal during the entire observation period (pre-mating, mating, post-mating, gestation and lactation periods).

The body weight gain was reduced with respect to controls in male and female animals at 600 and 200 mg/kg bw/day resulting in a slightly less body weight at 600 mg/kg bw/day in male animals from day 13 up to the termination and in female animals on gestation day 21 and lactation days 0 and 4. The summarized body weight gain also remained below the control value in male animals administered with 600 and 200 mg/kg bw/day and in females at 600 and 200 mg/kg bw/day during the pre-mating and at 600 mg/kg bw/day during the gestation period.

The mean daily food consumption was less comparing to the control group at 600 and 200 mg/kg bw/day doses during the pre-mating (male), during first week of pre-mating (female), on gestation weeks 2 and 3.



CONTAINS NO CBI

Hematology examinations revealed test item related higher percentage of reticulocytes in female animals administered with 600, 200 and 60 mg/kg bw/day and less hemoglobin concentration and hematocrit value at 600 mg/kg bw/day with respect to controls.

A higher mean activity of alanine aminotransferase and mean concentrations of urea referred to a test item influence on renal and/or hepatic function in female animals dosed with 600 mg/kg bw/day and 200 mg/kg bw/day. In male animals dosed with 600 mg/kg bw/day, the slightly elevated mean activity of alanine aminotransferase and higher concentration of creatinine and urea were also indicative of the test item effect.

Test item related renal changes (enlarged and pale kidneys) were observed in male animals dosed with 600 mg/kg bw/day. Specific macroscopic alterations related to the test item were not found in female animals during the necropsy.

Higher kidneys weights of male animals administered with at 600 and 200 mg/kg bw/day and higher liver weights in males at 600 mg/kg bw/day, in females at 600, 200 and 60 mg/kg bw/day reflected a test item influence on renal and hepatic functions in accordance with clinical chemistry and necropsy findings.

Test item related renal lesions (hyaline-like droplets in the epithelial cells of some proximal convoluted tubules, segmental tubular basophilia accompanied with slight intertubular lymphocytic infiltration and dilatation of tubuli in the distal part of tubuli) resembling on the "hyaline droplet nephropathy of male rats" were observed in all test item treated male groups (600, 200 and 60 mg/kg bw/day). The severity of lesions was less in the low dose group with respect to the middle or high dose groups. Hyaline droplet nephropathy was associated with interference to α -2 μ -globulin. In this case the observed nephropathy is specific to the male rat and has no relevance to humans.

There were no differences between the control and test item treated groups in the reproductive ability of male and female animals. Spermatogenesis in the rate male appeared unaffected by the test item. However, a test item influence on the dam's delivery appeared with respect to the controls at 600 mg/kg bw/day with a higher percentage of post-implantation loss and stillborns and higher numbers of dams with prolonged duration of pregnancy.

A test item effect on the offspring development was observed in the higher number and percentage of extra uterine mortality in 600 mg/kg bw/day group between postnatal days 0 and 4, and in the less litter weight and litter weight gain and mean pup's weight and weight gain at 600 and 200 mg/kg bw/day.

Conclusion:

Under the conditions of the present study, TBPND caused salivation, changes in body weight and food consumption and clinical pathology parameters (lower hemoglobin concentration and hematocrit value, and elevated percent of reticulocytes in female animals, higher mean activity of alanine aminotransferase and urea concentration in male and female animals, higher mean serum levels of creatinine in male animals), and changes in organ pathology (enlarged and pale kidneys, higher kidney weights and hyaline droplet nephropathy of male rats, higher liver weights in male and female animals) following an oral administration at 600 mg/kg bw/day to Hsd.Brl.Han:Wistar rats during the Combined Repeated Dose Toxicity Study with the Reproduction / Developmental Toxicity Screening Test.

This submission is not considered to be confidential. The item of concern is on the public list. Please contact me at (440)326-2419 if you have any questions regarding this letter.

Sincerely,



Mark J. King

Technical Director

Cc: Akzo Nobel Polymer Chemicals bv
Arkema France

Pergan GmbH
United Initiators GmbH & Co. KG



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