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8FHQ-06-16436	89100000279	7/19/10

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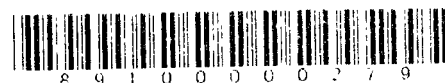
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DuPont Haskell Global Centers
for Health and Environmental Sciences
1090 Elkton Road, P.O. Box 50
Newark, DE 19714-0050

July 15, 2010

Via Federal Express

Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency, ICC Building
1201 Constitution Ave., NW
Washington, DC 20004



Dear 8(e) Coordinator:

8EHQ-06-16436/8EHQ-06-16478
2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propionic acid, ammonium salt

This letter is to inform you the preliminary results of an ongoing oral reproduction/developmental toxicity screening study in mice with the above referenced test substance. This test substance is subject to a Consent Order, PMN-08-509.

The objective of the study was to provide preliminary information on the potential adverse effects of the test substance on male and female reproduction. Test substance was administered once daily via oral gavage to groups of F₀ mice (CD-1; 25 per sex per dose group) at doses of 0 (deionized water), 0.1, 0.5, or 5 mg/kg/day at a dose volume of 10 ml/kg/day. Male mice (F₀) were dosed for a minimum of 70 days prior to mating and continued until the day of scheduled euthanasia. Female mice (F₀) were dosed for a minimum of 14 days prior to mating and continued throughout mating, gestation, and lactation until the day of scheduled euthanasia following weaning of offspring. For females that did not have positive signs of mating or delivery, dosing continued until the day of euthanasia. F₁ males and females were dosed beginning in postnatal day (PND) 21 until the day of euthanasia. Clinical signs, body weights, and food consumption were recorded throughout the study. At scheduled euthanasia, all animals underwent a gross external and internal examination; selected organs/tissues were weighed and/or retained for histopathologic examination. Reproductive performance was assessed by gonadal function, mating behavior, conception, parturition and lactation of the F₀ generation and the development of offspring from conception through day 40 of postnatal life. Developmental landmark data (vaginal patency and balanopreputial separation) was collected for F₁ offspring. Plasma samples for toxicokinetic analyses were collected from culled pups and pooled by litter on PND 4. Plasma samples for toxicokinetic analyses were prepared from a terminal bleed for F₀ females, weanlings that were not selected for developmental landmarks (PND 21), and weanlings designated for developmental landmarks (PND 40).

Full tabulation and summarization of the study data is in progress. The preliminary findings described below were based on summary data that are unaudited and pending full statistical analyses. In addition, the histopathologic examinations and toxicokinetic analyses are in progress.

At 5 mg/kg/day, a statistically significant increase in body weights/gains, food consumption, liver weights (42% in males and 102% in females) and kidney weights (8% in males, which is not statistically significant and 21% in females) compared to controls was observed in F₀ males and females. Offspring weights were lower, (3 and 6% for females and males, respectively), but not statistically significant than controls at birth. However, statistical significance for lower offspring body weight was evident beginning on PND 4 and persisting throughout lactation (15 to 24% lower than controls). Body weights remained lower until euthanasia on PND 40 but the magnitude of

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change diminished such that the mean final body weights on PND40 were 8% lower in males and 2% lower in females compared to controls. Mean day of achievement for preputial separation was 30.1 compared with 27.5 for controls. Mean day of achievement for vaginal patency was 30.0 compared with 26.6 for controls. These apparent differences in sexual maturation rates, however, are considered secondary to the body weight reductions at this dose level as these endpoints have been demonstrated to be sensitive to reductions in body weight and food consumption. (Carney et al., 2004 and Ashby and Lefevre, 2000) In addition, there are no differences in sexual maturation data at doses that did not result in lower body weights.

Test substance-related effects at 0.5 mg/kg/day included increased body weights/gains and food consumption (F₀ females) and increased liver weights (F₀ males – 26% and females – 24%).

There were no apparent test substance-related and adverse findings at 0.1 mg/kg/day.

Reproductive performance data including mating and fertility, gestation length, litter size and sex ratio at birth, postnatal survival throughout lactation including instances of whole litter losses were all generally comparable to the control group data at all doses tested.

This information is submitted in accordance with current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act or, where it is not clear that reporting criteria have been met, it is submitted as a precautionary measure and because it is information in which EPA may have an interest.

Sincerely,



A. Michael Kaplan, Ph.D.
Director - Regulatory Affairs

AMK/SM: clp
(302) 366-5260

References:

Carney, E.W. et al., (2004) The Effects of Feed Restriction During *in Utero* and Postnatal Development in Rats, *Toxicological Sciences* 82, 237-249.

Ashby, J. and P.A. Lefevre (2000) The Peripubertal Male Rat Assay as an Alternative to the Hershberger Castrated Male Rat Assay for the Detection of Anti-androgens, Oestrogens and Metabolic Modulators, *Journal of Applied Toxicology* 20, 35-47.

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