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DOCUMENT DESCRIPTION	DOCUMENT CONTROL NUMBER	DATE RECEIVED
8EHQ-06-16436	89130000231	1/9/13

COMMENTS: 8EFU

DOES NOT CONTAIN CBI

MR#350977

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

January 8, 2013

Via Federal Express

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Document Processing Center (Mail Code 7407M)
Room 6428
Attention: 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
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
CAS # 62037-80-3

This letter is to inform you of the preliminary results of a 2 year rat oral gavage study with the above referenced test substance. This test substance is subject to a Consent Order, P-08-509.

A 2-year oral gavage study was conducted in Crl:CD(SD) rats (80/sex/concentration) with the test substance at doses of 0, 0.1 (males only), 1, 50, and 500 (females only) mg/kg bw/day. The rats were evaluated for mortality, clinical signs, body weight and weight gain, food consumption, and food efficiency, and received an ophthalmology examination pretest and after 1 and 2 years of dosing. Ten rats/sex/dose were designated for evaluation of chronic toxicity. These rats were evaluated for clinical pathology at 3, 6, and 12 months, and for anatomic pathology (organ weights, gross and microscopic pathology) at the end of 12 months. The remaining rats (70 rats/sex/dose; main study rats) were dosed for up to 23 (females) or 24 (males) months. Females were sacrificed at week 100 due to poor overall survival, although survival was comparable among all dose groups. Clinical pathology (WBC differential counts) was evaluated at 12, 18, and 24 months in all surviving main study rats. All animals received a gross pathology evaluation at necropsy, and organ weights were collected in animals surviving to terminal sacrifice. Microscopic examination of tissues was conducted in animals that survived to scheduled sacrifice (12 month and end of study), and in all animals that died prior to scheduled sacrifice.

No test substance-related differences in survival or in clinical or ophthalmological signs were observed in any dose group. No adverse effects on overall body weight and nutritional parameters were observed in any dose group, although these parameters were transiently lower than control (statistically significant) in high-dose males (50 mg/kg/day) and females (500 mg/kg/day) over some weekly/biweekly intervals, particularly during the middle of the study. In 500 mg/kg/day females, the body weight over the first year of the study was statistically significantly lower than in control, although the difference was not statistically significant at the end of two years. Test substance-related, adverse or potentially adverse findings were observed in some clinical and anatomic pathology parameters in females at 500 mg/kg/day and in males at 50 mg/kg/day parameters, as discussed below.

Clinical pathology: The following statistically significant differences were considered adverse:

500 mg/kg/day (females only):

- ↓ red blood cell mass parameters (RBC, HGB, HCT, most time points), with ↑ MCV and reduced MCHC at the 12 month time point.
- ↑P (12 month), ↑ BUN (12 month), ↑A/G ratio (all time points), ↓globulin (all time points),

CONTAINS NO CBI

- urine: ↑urine volume and pH, ↓specific gravity (6, 12 month)

50 mg/kg/day:
- ↑ALP (male all time points), ↑ALT (male 12 month), ↑albumin (male all time points), ↑A/G ratio (male all time points)

Anatomic pathology: Increases in the following microscopic pathology findings were considered adverse:

500 mg/kg/day (females):
- Liver: adenoma, hypertrophy (also ↑ at one year), degeneration and necrosis; ↑ liver weight (at one and two year)
- Kidney: papillary necrosis and edema, chronic progressive nephropathy (also ↑ at one year), dilated tubules,
- Stomach: non-glandular mucosal hyperplasia
- Tongue: mucosal hyperplasia/inflammation

50 mg/kg/day:
- Liver: ↑ liver weight (males at one year only), hypertrophy, degeneration and necrosis (also ↑ in males at one year), basophilic foci; (males only except hypertrophy)
- In males, marginal increases were observed in the following:
  - Pancreas: acinar cell tumors; equivocal acinar cell hyperplasia (both sexes)
  - Testes: interstitial cell tumors and hyperplasia

All other statistically significant changes in clinical and anatomic pathology parameters were considered spurious and/or nonadverse based on absence of a dose response, the transient occurrence of the finding, the minimal nature or direction of the change, and/or the lack of correlative changes in related parameters. These included:

500 mg/kg/day (females only)
- ↑ Cl (6 month), ↑albumin (3 month), ↓bilirubin (all time points), ↓total protein (3 month), ↓ cholesterol (6 month), ↓APTT (12 month)
- Uterus: stromal polyps (not significant by Fisher's exact test and within historical control range)
- Lung: histiocytosis (within historical control range)
- Adrenal: benign pheochromocytoma (not significant by Fisher's exact test, within historical control range and not associated with correlative increase in hyperplasia)

50 mg/kg/day:
- ↓red blood cell mass parameters (RBC, HGB, HCT) at all time points in males; ↓RBC in females (12 month)
- ↓APTT (12 month; female))
- ↑ Ca (male 12 month), ↑P (male 3 month), ↑A/G ratio (female 3 and 6 month), ↓globulin (female 6 month)
- Urine: ↓urine volume (male 12 month) and pH (male 6 and 12 month)

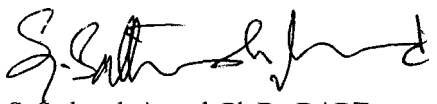
1 mg/kg/day:
- ↓HGB (female 3 month), ↑ALP (male 12 month), ↑ BUN (male 12 month), ↑albumin (male 12 month), ↑A/G ratio (male all time points), ↑Cl (female 6 month)
- Urine: ↑urine volume (male 12 month) and pH (male 6 and 12 month; female 6 month)

0.1 mg/kg/day (males only):
- ↑P (3 month)
- Urine: ↓urine volume and ↓ pH (both 12 month)

Under the conditions of this study, the no-observed-adverse-effect level (NOAEL) was considered to be 1 mg/kg/day in male and female rats. Test substance-related neoplastic changes were observed at the high dose (500 mg/kg/day in females; 50 mg/kg/day in males) and included hepatocellular tumors in females and, in males, equivocal increases in pancreatic acinar cell tumors and testicular interstitial cell tumors. These tumor findings are typical of those previously reported in rats following exposure to other PPARα agonists. Based on the high dose threshold for these tumor responses in this study, the lack of genotoxicity of the test material across a battery of *in vitro* and *in vivo* tests, and the known responses of the rat versus other species, including humans, to these PPARα-associated tumor responses, these tumor findings are not considered relevant for human risk assessment.

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,



S. Satheesh Anand, Ph.D., DABT
Senior Research Toxicologist

SSA/SAM: jhh
(302) 366-5314

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