Data Evaluation Record

FENVALERATE
PC Code ~~109303~~

EPA Contract No. EP10H001452
Task Assignment No. 1-33-2010

Study Type: Non-Guideline

Citation: Moniz, A. et al. (1999) Perinatal fenvalerate exposure: behavioral and endocrinology changes in male rats. *Neurotoxicology and Teratology* 21(5): 611-618.

Prepared for
Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard
2777 S. Crystal Drive
Arlington, VA 22202

Prepared by
Dynamac Corporation
1910 Sedwick Road,
Building 100, Suite B
Durham, NC 27713

Primary Reviewer
David A. McEwen, B.S.

Signature: David A. McEwen
Date: 12/14/2010

Secondary Reviewer
Tracy S. Lang, M.S.

Signature:
Date: 12/16/2010

Program Manager:
Jack D. Early, M.S.

Signature: Jack D. Early
Date: 12/16/2010

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EPA Reviewer: Gregory Akerman **Signature:** _____
Risk Assessment Branch I, Health Effects Division (7509P) **Date:** _____

EPA Secondary Reviewer: Jess Rowland **Signature:** _____
Immediate Office, Health Effects Division (7509P) **Date:** _____

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Data Evaluation Record

TXR No: 0055634

STUDY TYPE: Non-guideline

DP BARCODE: D379859

PC CODE: 109301

CAS NO.: 51630-58-1

MRID NO.: 48233808

TEST MATERIAL: Fenvalerate (purity not reported)

CITATION: Moniz, A.; Cruz-Casallas, P.; Oliveira, C.; Lucisano, A.; Florio, J.; Nicolau, A.A.; Spinosa, H.; and Bernardi, M. (1999) Perinatal fenvalerate exposure: behavioral and endocrinology changes in male rats. *Neurotoxicology and Teratology* 21(5): 611-618.

SPONSOR: This journal article was submitted as "Other Scientifically Relevant Information" (OSRI) in response to the Agency's Test Order for Tier 1 screening assay for the Endocrine Disruptor Screening Program.

EXECUTIVE SUMMARY: The purpose of the study (MRID No. 48233808) was to investigate the effects of maternal fenvalerate exposure during the prenatal and postnatal periods of sexual brain differentiation in adult male offspring. Behavioral (open-field, stereotyped, and sexual behaviors), physical (sexual maturation and body and organ weights), endocrine (testosterone levels), and neurochemical (striatal and hypothalamic monoamine and respective metabolite levels) data were assessed.

Forty sexually naïve female Wistar rats (approximately 90 days old and weighing between 250-270 g) were mated with males previously shown to be fertile (2 females:1 male/cage). Pregnancy was determined by vaginal smear test. Fenvalerate was administered via intraperitoneal injection (IP) to 20 pregnant dams at a concentration of 10 mg/kg on gestation day (GD) 18, post-natal day (PND) 1 (during the first 10 minutes after delivery before the dam started nursing), and once per day from PND 2-5. Additionally, a control group of 20 dams was similarly treated with saline alone (1 mL/kg IP).

After delivery, all litters were examined externally, sexed, and weighed. Litters were culled to 8 pups/litter (4/sex) and remained with their dam until weaning, PND 21. Male pups were checked daily for testis descent and were weighed on PND 1, 10, 21, and 60.

On PND 120, control and treated males were submitted to mating tests, open field studies, and stereotypy studies according to previously published methods. In mating tests, the following parameters of male sexual behavior were recorded: mounts, intromissions, and ejaculatory latencies; number of mounts and intromissions until the first ejaculation; number of mounts, intromissions, and ejaculations over a 40-minute period; and post-ejaculatory mounts and intromission latencies after the first ejaculation. Copulatory efficiency, sexual activity index, and neuromotor index were calculated. In open-field testing, rats were scored for ambulation, rearing frequency, and immobility duration during a 3-minute observation period. For stereotypy testing, control and treated animals were injected with 0.6 mg/kg of apomorphine (subcutaneous) and observed for stereotypic behavior in the home cage. Stereotypic behavior was quantified at 10 minutes after injection and every 10 minutes during a 90-minute observation period. Animals were scored on a scale of 0 (asleep or stationary) to 6 (continuous licking or gnawing of cage grid). The sum of scores obtained during the 60-minute period following administration was used to evaluate stereotypy intensity.

On PND 120, testes, seminal vesicles, and ductus deferens were removed, and organ weight/body weight ratios were calculated for control and treated males (n = 10 for controls; 14 for treated); testes were analyzed for histopathological alterations. Separate control and treated groups (n = 10/group) were weighed and decapitated, and trunk blood was collected. Plasma testosterone concentration was measured in plasma samples using commercial radioimmunoassay kits. Serum samples were assayed in duplicate, and sensitivity of testosterone was found to be 0.01 ng/mL. The intra-assay and interassay variation was 0.4% and 4.5%, respectively.

On PND 140, control and treated animals were decapitated. Brains were dissected on dry ice; striatum and hypothalamus were weighed and stored at -70 ºC. For analysis, perchloric acid was added to the tissues, and the tissues were homogenized by sonication 1 week prior to neurochemical evaluations. Striatal and hypothalamic monoamine and metabolite levels were determined.

Data were first analyzed using Bartlett's test for homogeneity of variance. Parametric data were analyzed using the Student *t*-test, while non-parametric data were analyzed using the Mann-Whitney U-test. Significance was denoted at $p<0.05$.

Perinatal exposure to fenvalerate caused significant ($p<0.05$) decreases in offspring body weights on PND 21 and 60. During the sexual behavior studies, treated males displayed a significant increase in total number of mounts until ejaculation (22.6 ± 2.7 treated vs. 15.8 ± 1.1 controls) and a decrease in the number of ejaculations during 40 minutes (2.0 ± 0.3 treated vs. 3.0 ± 0.2 controls). The copulatory efficiency, sexual activity, and intromission frequency/minute, as well as the stereotyped behavior of treated animals were similar to controls. The duration of immobility was increased during the open-field observations; however, no differences in

locomotion or rearing frequencies were observed. Testosterone levels were decreased, and seminal vesicle and prostate weights were decreased; however, no changes in the age of testes descent or in testis or ductus deferens weight were observed. Striatal and hypothalamic monoamine and metabolite levels were similar to controls.

The study was conducted by the Department of Pathology, University of São Paulo (São Paulo, Brazil) and was reported according to the standards of the journal *Neurotoxicology and Teratology*.

CLASSIFICATION: Not Applicable. This study does not conform to a recognized guideline requirement. The qualitative information provided in this study is considered to be acceptable for use during a weight-of-evidence evaluation of the OSRI.