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COMPANY SANITIZED

8EHQ-0405-158895



**Attn:** TSCA §8(e) SUBMITTAL

Re: TSCA 8(e) Submittal **8EHQ-05-15889** for tetrapropenyl phenol

is submitting this notice pursuant to Section 8(e) of the Toxic Substances Control Act (TSCA).

A one-generation rat reproductive toxicity study was conducted according to OECD testing guideline 415 specifications. The study was designed to exceed guideline requirements. Each group consisted of 30 males and 30 females per dose level. Male and female rats (F<sub>0</sub> generation) were administered Tetrapropenyl Phenol by daily gavage at dose levels of 0 (corn oil vehicle), 5, 25, and 125 mg/kg/day for ten weeks prior to mating, throughout mating, gestation and lactation. Estrus evaluation, via vaginal smearing, was conducted during the last three weeks prior to mating (study weeks 7 - 10). Semen evaluation was conducted on males at necropsy. Two pups/sex/litter (where possible) were randomly selected at weaning for evaluation of age and weight at vaginal opening or preputial separation. These selected pups were not dosed during the post-weaning period. Non-selected pups were necropsied at weaning on postnatal day 21. Microscopic evaluation of control and high dose organs has just been completed. All data are in unaudited draft form.

Our previous 8(e) submission reported the following reproductive findings at 125 mg/kg/day: altered estrus cyclicity, reduced gestation body weight change, fewer litters produced, reduced litter size, and reduced pup viability.

This supplemental submission is to report additional findings from the study. Due to the reduced number of litters at 125 mg/kg/day, offspring parameters at the high dose were limited to N = 1 or 2; therefore, no conclusions have been drawn from the offspring results at the high dose.

At 25 mg/kg/day, pup body weight gain was reduced in both male and female offspring from postnatal day (PND) 4 through PND 21, resulting in statistically lower pup body weight on PND 14 and 21. Post-weaning, male offspring body weight gain continued to be reduced through PND 35, and male body weight was statistically lower than control through PND 42. In female offspring, there were no differences in post-weaning body weight gain, although there was a lingering difference in body weight through PND 35. No effects occurred at 5 mg/kg/day. There



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were no effects upon dam lactation body weight or lactation body weight change; at the high dose, the data are limited by the small number of litters produced.

No effects occurred upon age at vaginal opening or mean body weight at vaginal opening. Preputial separation was delayed in males at 25 mg/kg/day, although there was no effect upon body weight at preputial separation, suggesting overall developmental delay.

At the time of female necropsy, high dose females weighed less than their control counterparts (81.5% of control). Some portion of this difference is likely due to the difference between the groups in reproductive status. Necropsy of the F<sub>0</sub> females revealed a reduction in implantation sites at 125 mg/kg/day. Reduced organ weights were noted at 25 mg/kg/day and 125 mg/kg/day for the liver, ovaries/oviducts, and thyroid; spleen weight was reduced at 125 mg/kg/day. Due to the difference in final body weight, the relative weight of many organs was statistically greater than the control values. Microscopic examination at the high dose level shows kidney mineralization, ovarian cysts and reduced corpora lutea, endometrial gland cysts and reduced implantation sites in the uterus, fewer females with mammary gland hyperplasia (most did not become pregnant and therefore didn't lactate), and differences in estrus cycle stages were confirmed in the vaginal tissues (more high dose females in estrus).

In males, body weight at necropsy was reduced at 25 mg/kg/day and 125 mg/kg/day by 9.9% and 25.7%, respectively. Seminal vesicle/coagulating gland weights, both absolute and relative, were reduced at all dose levels. Other male organ weights (prostate, epididymides, testes, thymus, liver) were reduced on an absolute basis but not relative to body weight. Adrenal and pituitary weights were increased at 25 mg/kg/day and 125 mg/kg/day. There were no effects upon sperm motility, testicular sperm concentration, or sperm morphology; however, epididymal sperm concentration was reduced at 125 mg/kg/day.

Additional microscopic evaluation of tissues to determine no-effect levels for each organ will be conducted in the near future. As with the earlier submission, all data are still in unaudited draft form. When the final report is completed, it will be submitted to you.

If you have any questions, please direct them to

Sincerely,