The absolute weights of the brain, liver, kidneys, adrenals, spleen, thymus, ovaries and uterus and the ratios of these organ weights to the terminal body weight and the brain weight were unaffected by dosages of the test substance as high as 30 mg/kg/day.

Primordial follicle count for ten F1 generation female rats in the vehicle control and 30 mg/kg/day dosage groups were comparable and did not significantly differ.

B.8. Histopathology (APPENDIX K)

No treatment-related microscopic changes were observed in the reproductive organs of any of the 10 female rats in the F1 generation selected for histopathologic evaluation that had been given up to 30 mg/kg/day of the test substance. All microscopic changes observed in the various organs and tissues were considered to have occurred spontaneously and to be incidental and unrelated to treatment. There were a few microscopic changes observed in rats designated as “reduced fertility”, but these changes occurred spontaneously and were of the type that occur spontaneously in female rats of the age and strain and were not compound-related.

B.9. Natural Delivery and Litter Data - F1 Generation Female Rats (Summaries - Tables E20, E21 and E25; Individual Data - Tables E38 through E41 and E45)

Pregnancy occurred in 28 to 29 rats in each dosage group. Natural delivery observations were unaffected by dosages of the test substance as high as 30 mg/kg/day. Values for the numbers of dams delivering litters, the duration of gestation, averages for implantation sites per delivered litter, the gestation index (number of dams with one or more liveborn pups/number of pregnant rats), the numbers of dams with stillborn pups, dams with all pups dying and liveborn and stillborn pups were comparable among the five dosage groups and did not significantly differ.

The viability index (number of live pups on day 5 postweaning per number of liveborn pups on day 1 postweaning) and lactation index (number of live pups on day 22 postweaning per number of live pups on day 5 postweaning) were comparable and did not differ significantly.

The numbers of pups found dead or presumed cannibalized were significantly increased (p≤0.01) in the 3 and 10 mg/kg/day dosage groups on day 1 of lactation. These increases were not considered related to the test substance because: 1) they were not dosage-dependent; and 2) they did not affect any other measures of pup viability (surviving pups per litter, live litter size at weighing).

The number of pups surviving per litter, the percentage male pups, litter size and average pup body weight per litter were comparable and did not differ significantly on DLs 1, 5, 8, 15 or 22 for any of the dosage groups when compared to the control group. Anogenital distances measured for male and female pups on DLs 1 and 22 were comparable among the five dosage groups and did not significantly differ.