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EXXON BIOMEDICAL SCIENCES, INC.

FINAL REPORT

PROJECT NUMBER: 283937-I

TEST MATERIAL: MRD-86-839

DETERMINATION OF MATERNAL TOXICITY AND FETAL TOXICITY OF BENZENE IN RATS FOLLOWING ORAL EXPOSURE

PERFORMED AT:

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SUMMARY

The test material, MRD-86-839, was administered by oral gavage to mated female Sprague-Dawley rats from day 6 to day 15 of gestation (G) at dose levels of 0, 50, 250, 500, or 1,000 mg/kg. Body weight and food consumption were measured and physical examinations performed during gestation. Mated females which survived to day 20G were sacrificed, and a gross necropsy was performed on all mated females. Intact uteri with ovaries attached were weighed. Uterine contents were examined for the number of implantation sites, early and late resorptions, live and dead fetuses. For animals sacrificed on day 20G, corpora lutea were counted. Full term fetuses were examined for external abnormalities, and fetus weight was measured.

The most common in-life observation noted was alopecia on the hindquarters, lateral lumbar areas, abdominal, inguinal, and ventral thoracic and cervical areas. This was seen in the 50, 250, 500 and 1000 mg/kg groups and was significantly higher than control in the 1000 mg/kg group.

Maternal body weight change during gestation was decreased in response to dose of the test material. Maternal weight change was most reduced after the initiation of dosing (days 6-9G) with the 500 mg/kg and 1000 mg/kg groups significantly different from the control group. Depression of weight gain was less severe for the remainder of treatment (days 9-12G, 12-16G), and following treatment, the test material exposed groups gained more weight than the control group.

Maternal food consumption was a more sensitive indicator of maternal toxicity because significant decreases relative to control were evident for the 250 mg/kg group as well as the 500 mg/kg and 1000 mg/kg groups. For these groups food consumption was significantly decreased for the intervals days 6-9G, 9-12G, and, for the 500 and 1000 mg/kg groups only, days 12-16G. Thus, depression of food consumption was observed at a lower dose level and persisted longer compared to the depression of maternal body weight gain.

Necropsy observations for animals surviving to day 20G were unremarkable.

There were no statistically significant differences among the dose groups for pregnancy rate or numbers of live fetuses, resorptions, implantations, corpora lutea, fetuses per implant or resorptions per implant.

There were no dead fetuses in this study, and no external malformations were observed in term fetuses.

SUMMARY (continued)

Analyses of live fetal body weight revealed that both male and female fetuses in the 500 mg/kg and 1000 mg/kg groups had significantly lower body weights than control.

In sum, under the conditions of the experimental methods, MRD-86-839 was toxic to maternal Sprague-Dawley rats at dose levels of 250, 500, and 1000 mg/kg as evidenced by decreased food consumption during gestation. Decreased fetal bodyweight was observed at dose levels of 500 and 1000 mg/kg concurrently with decreased maternal food consumption and decreased maternal weight gain during gestation.