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Oral Developmental Toxicity (Teratology) in Rats and Rabbits

An oral teratology study in rats with potassium perfluorooctanesulfonate was conducted at Riker Laboratories (Riker Pharmaceutical Pathology / Toxicology Laboratory). Dose levels (oral) given to the pregnant rat dams were 0, 1, 5, and 10 mg/kg. Maternal toxicity (reduced weight gain) occurred at the high dose of 10 mg/kg on days 6 through 15 of gestation. Evidence of fetal toxicity was not found at any dose level. No skeletal and soft tissue teratogenic changes were found at any dose level with one exception. A change in the lens of the eye was found in all dose groups including the control but the incidence in high dose group was significantly higher. This change was reported as a developmental eye abnormality and the summary of the report states the compound was teratogenic. An outside consultant and teratology expert, Dr. E. Marshall Johnson from Jefferson Medical College, visited 3M and reviewed the rat pup eye specimens in question. He concluded that the eye/lens changes were, in fact, sectioning artifacts and not compound related teratology abnormalities (see enclosed letter). A repeat study was conducted at Hazleton Laboratories America (see below) which revealed no effects on the lens.

In the subsequent study mentioned above, potassium perfluorooctanesulfonate (suspended in corn oil) was administered on gestational days 6-15 by oral gavage to groups of 25 pregnant Sprague-Dawley CD rats at doses of 0 (control), 1, 5, and 10 mg/kg/day (Hazleton Laboratories America). Severe maternal toxicity occurred in the 5 mg/kg and 10 mg/kg dose groups, as evidenced by significant reductions in mean body weight gain, terminal body weight minus gravid uterine weight and food consumption compared to control dams, actual losses in body weight on commencement of treatment among numerous dams and death in two dams in the 10 mg/kg dose group prior to gestational day 20. Mean body weight gains (days 0-20) at 5 and 10 mg/kg were 104 ± 35 (S.D.) and 34 ± 73 (S.D.), respectively, as compared to 125 ± 24 (S.D.) in the control group. Mean food consumption values (days 0-20) at 5 and 10 mg/kg were 363 ± 60 (S.D.) and 264 ± 90 (S.D.), respectively, as compared to 421 ± 28 for the control group. Mean terminal body weight minus gravid uterine weight at 5 and 10 mg/kg was 293 ± 28 (S.D.) and 241 ± 60 (S.D.), respectively, as compared to 321 ± 23 (S.D.) in the control group. Clinical signs in surviving dams included hunching, lower body weight, alopecia, rough haircoat, anorexia. Gastrointestinal and kidney lesions were noted in the high-dose dams.
Treatment-related fetal effects that were attributed to maternal toxicity included: increased resorptions and fetal death, decreased fetal body weight, delayed skeletal

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ossification, cleft palate, subcutaneous edema and cryptorchism (undescended testicles). These effects occurred primarily in the high-dose group. The maternal and fetal NOAELs for this study were both 1 mg/kg/day.

An oral developmental toxicity (teratology) study in rabbits was conducted at Argus Laboratories. In this study, dose groups of 22 pregnant new zealand white rabbits were dosed on days 7 through 20 of gestation with either 0, 0.1, 1.0, 2.5, or 3.75 mg/kg/day PFOS.

Maternal toxic effects included: 1) decreased body weight at the highest three dose levels with a minimal effect at the 1.0 mg/kg dose; 2) decreased food consumption at the highest two doses; 3) frequent scant feces at the highest dose, and 4) increased abortions at the highest two doses.

Fetal toxic effects included reduced fetal weight and an increase in delayed ossification at the highest two doses. No teratogenic events were observed in the study.

Based on this study, PFOS was not teratogenic under conditions of the study and the maternal and fetal NOELs are 0.1 mg/kg/day and 1.0 mg/kg/day, respectively.

Thus, the weight of the evidence indicates that perfluorooctanesulfonate does not cause teratogenic effects in rats and rabbits when dosed at levels which are not maternally toxic. The lens change observed in rat pups in the Riker Pharmaceutical study was a sectioning artifact and was not found upon repeat studies at an independent laboratory.