Summary of the Heindel et al. (1992) study

In this guide

This is a paper for discussion. This does not represent the views of the Committee and should not be cited.

14. While the Heindel et al. (1992) paper states only conduct under contract to the National Toxicology Program and the National Institute of Environmental Health Sciences (NTP/NIEHS), the follow up paper (Price et al. 1996) reports funding under the sponsorship of U.S. Borax Inc.

15. Heindel et al. (1992) conducted studies involving timed-mated Sprague-Dawley rats (29 per group) fed diets containing 0, 0.1, 0.2, or 0.4% boric acid from gestation day (GD) 0 to 20. The estimated boric acid doses were 0, 78, 163, and 330 mg/kg bw/day (0, 13.6, 28.5, and 57.7 mg B/kg bw/day). Additional groups of 14 rats received 0 or 0.8% boric acid (539 mg/kg bw/day or 94.2 mg B/kg bw/day) from GD 6 to 15 to minimize preimplantation loss and early embryo lethality identified in preliminary studies. Monitoring included food and water intake, body weights, and clinical toxicity signs throughout pregnancy. On GD 20, the animals were sacrificed, and organ weights, uterine contents, and maternal kidney histology (10 randomly selected dams/group) were evaluated. Fetal examination included assessment of weight, external and visceral malformations, and skeletal anomalies, with significance set at $p < 0.05$.

16. **Maternal Findings:** There was no maternal mortality observed. On GD 12-20, food intake increased by 5-7% at 0.2% and 0.4% boric acid, whereas water consumption remained unaffected. Food and water intake decreased at 0.8% on GD 6–9 and increased on GD 15–18. Treatment had no effect on the pregnancy rates (90–100%). Increased relative liver and kidney weights (0.2% and higher), increased absolute kidney weight (0.8%), and reduced body weight gain (0.4% and higher) were among the dose-related maternal effects. Corrected body weight gain was unaffected except for an increase at 0.4%. Maternal kidneys showed minimal nephropathy, but it was not dose dependent.

17. **Fetal Findings:** Prenatal mortality increased at 0.8% boric acid, with more resorptions and late fetal deaths per litter, and fewer live fetuses per litter. Fetal body weight decreased in a dose-dependent manner, with weights at 94%, 87%, 63%, and 46% of controls for 0.1%, 0.2%, 0.4%, and 0.8%, respectively. Malformations were significantly increased at 0.2% and higher, primarily affecting the eyes, CNS, cardiovascular system, and axial skeleton. Common malformations included brain ventricle enlargement and rib XIII agenesis/shortening. Skeletal variations such as wavy ribs were observed, especially at 0.8%.

18. The authors concluded a maternal LOAEL of 0.2% boric acid (28.5 mg B/kg bw/day), with a maternal NOAEL of 0.1% (13.6 mg B/kg bw/day) and a fetal LOAEL of 0.1% boric acid (13.6 mg B/kg bw/day), with no NOAEL identified.