SUMMARY

Background: Tris(chloropropyl) phosphate (TCPP) is a chemical used as a flame retardant in many consumer products, including textiles and furniture foam, as well as construction materials. It has been proposed as a replacement for brominated flame retardants, and its use as a flame retardant in home furnishings and construction materials is expected to increase. Humans are exposed to TCPP primarily through inhalation of vapors or dust, direct skin contact, and/or ingestion of contaminated food throughout the lifespan,

including during pregnancy and early childhood. The effects of exposure to TCPP in male and female rats (starting in utero and continuing till the end of life) and male and female mice (starting in adolescence) were studied to identify potential toxicity or cancer-related outcomes.

Methods: Pregnant rats were fed diets containing 2,500, 5,000, 10,000, or 20,000 parts per million (ppm) TCPP throughout pregnancy and during the nursing of their offspring; afterwards, groups of 50 male and 50 female rat offspring continued the same diet as their mothers for 2 years. Fifty male and 50 female mice were fed diets containing 1,250 (males only), 2,500, 5,000, or 10,000 (females only) ppm TCPP for 2 years beginning in adolescence. Additional 3-month studies were conducted to set appropriate doses and identify target organs for subsequent studies. Control animals (rats and mice) for all studies were fed diets with no chemical added (0 ppm TCPP). Tests were conducted to evaluate the potential for TCPP to cause DNA damage. At the end of each study, tissues from more than 40 sites from every animal were examined for signs of disease.

Results: Exposure of pregnant rats to TCPP had no discernable effect on their health. However, while nursing their offspring, body weights were reduced in the rats in the highest exposure group (i.e., 20,000 ppm). Rat offspring of the highest exposure group also had reduced body weight. In the rat and mouse offspring exposed for 2 years, neoplasms (which can include benign or malignant growths) were observed in the liver and in the uterus of female rats. Other effects observed in male and female rats and female mice exposed to TCPP included noncancerous tissue abnormalities in the liver. Male mice did not have exposure-related noncancerous lesions in any examined tissue. Tests to evaluate the potential **TCPP** for to damage DNA were negative.

Conclusions: The NTP four-point scale rates the level of evidence that a substance has the ability to cause cancer in laboratory animals. Under the conditions of these 2-year feed studies, there was clear evidence that TCPP exposure has the ability to cause liver cancer in female mice, some evidence that it has the ability to cause liver cancer in male rats and male mice and uterine cancer in female rats, and equivocal (uncertain) evidence that it has the ability to cause liver cancer in female rats. In addition, TCPP exposure caused increased incidences of noncancerous tissue abnormalities in the liver of male and female rats and female mice, and in the kidney of male mice.

