NTP Technical Report on the Toxicology Studies of Tetrabromobisphenol A (CASRN 79-94-7) in F344/NTac Rats and B6C3F1/N Mice and Toxicology and Carcinogenesis Studies of Tetrabromobisphenol A in Wistar Han [Crl:WI(Han)] Rats and B6C3F1/N Mice (Gavage Studies)

SUMMARY

Background: Tetrabromobisphenol A (TBBPA) is used as a flame retardant in circuit boards and in enclosures for electronics. Studies have shown that these products release TBBPA into the environment; thus, human exposure occurs via ambient air, dermal contact, and ingestion, as well as during the disposal, recycling, incineration, and landfilling of electronic waste. No adverse effects in humans have been reported following TBBPA exposure,



and no irritation or allergic reactions have been documented. The effects of oral administration of TBBPA in male and female rats and mice were studied to identify potential toxicity or cancer-related outcomes.

Methods: Groups of 50–60 male and 50–60 female rats and mice were orally administered 250, 500, or 1,000 milligrams (mg) of TBBPA per kilogram (kg) of body weight in corn oil via oral gavage. Control animals received 0 mg/kg (corn oil alone). Animals were administered TBBPA 5 days per week for 2 years. Additional groups of animals were evaluated for organ weights after 3 months, and additional 3-month studies were conducted to set appropriate doses and identify target organs for subsequent studies. Tests were conducted to evaluate the potential for TBBPA to cause DNA damage. At the end of the study, tissues from more than 40 sites from every animal were examined for signs of disease.

Results: Survival was decreased in male and female mice administered the highest dose of TBBPA. Body weights were decreased in male rats administered the two highest doses and female mice administered the highest dose. Male rats administered 1,000 mg/kg of TBBPA for 2 years had an increased incidence of neoplasms (which can include benign or malignant growths) of the testis. In female rats, there were significant increases in the incidences of neoplasms of the uterus. In male mice, there was a significant increase in the incidence of liver neoplasms, as as the incidence of well hemangiosarcoma (a malignant cancer related to blood vessels) and neoplasms of the large intestine. Other effects observed included noncancerous tissue abnormalities in the endometrium (a tissue that lines the uterus) and ovary of female rats, liver and kidney of male mice, and the forestomach (a tissue that stores undigested food) of male and female mice. Tests to evaluate the potential for TBBPA 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 gavage studies, there was clear evidence that TBBPA exposure has the ability to cause uterine cancer in female rats, some evidence that it has the ability to cause liver cancer in male mice, equivocal (uncertain) evidence that it has the ability to cause testis neoplasms in male rats and large intestine neoplasms and hemangiosarcoma in male mice, and no evidence that it has the ability to cause cancer in female mice. In addition, TBBPA exposure caused increased incidences of noncancerous tissue abnormalities in the uterus and ovary in female rats, the liver and kidney in male mice, and the forestomach in male and female mice.

