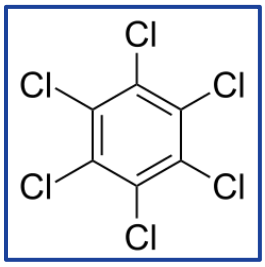
SUMMARY

Background: Hexachlorobenzene (HCB) was used in the United States as a fungicide and wood preserving agent as well as in the manufacture of aluminum and rubber until it was phased out in 1984. However, HCB is still released into the environment as a byproduct of several pesticides and during incineration of municipal waste. Due to its persistence in the environment, there is the potential for chronic, low-dose exposure in humans. The effects of low-dose exposure to HCB were studied in adult female rats to identify potential toxicity in humans.



Methods: Groups of 10 female rats were orally administered 0.03, 0.1, 0.3, 1, 3, 10, or 25 milligrams (mg) HCB/kilogram (kg) body weight/day in a mixture of corn oil and acetone for 3 months. Control animals were given the corn oil and acetone mixture with no HCB added (0 mg/kg/day HCB). At the end of the study, body and organ weights were measured, blood was collected for thyroid hormone analysis, and livers and lungs were collected to measure cytochrome P450 activity (enzymes involved in metabolism). Tissues from approximately 20 sites from every animal were examined for signs of disease. Additional studies were conducted to determine whether HCB has the ability to cause DNA damage and to identify the elimination half-life of HCB in the blood (the amount of time for the concentration of HCB in the blood to decrease by half). In addition, the toxicity of HCB was evaluated relative to that of another highly toxic chemical, 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), using data from a previous NTP study (Technical Report 521).

Results: Rats administered 25 mg/kg/day HCB had increased body weights at the end of the study compared to the control group. Increased spleen, liver, lung, and kidney weights were also observed. Thyroid hormones (thyroxine and triiodothyronine) were decreased, whereas cytochrome P450 activities were increased in the liver and lung. The effects that HCB had on thyroid hormone concentrations and cytochrome P450 activities in the liver and lung were different from the effects TCDD had on these outcomes. Noncancerous tissue abnormalities were observed in the liver, lung, spleen, mammary gland, skin, thymus, and teeth and increased in incidence in a dose-related manner (the effects increased as the dose increased). Tests evaluating the potential for HCB to damage DNA were negative. The elimination half-life of HCB was determined to be between 48 and 53 days.

Conclusions: *Under the conditions of this 3-month study, oral administration of HCB resulted in dose-related noncancerous tissue abnormalities in the liver, lung, spleen, mammary gland, skin, thymus, and teeth of female rats. Dose-related decreases in thyroid hormones were also observed, although these were not accompanied by tissue abnormalities in the thyroid gland.*