

## Dioxin-like Effects Observed in Male Rats following Exposure to Octachlorodibenzo-*p*-Dioxin (OCDD) during a 13-Week Study<sup>1</sup>

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Dioxin-like Effects Observed in Male Rats following Exposure to Octachlorodibenzo-*p*-dioxin (OCDD) during a 13-Week Study. COUTURE, L. A., ELWELL, M. R., AND BIRNBAUM, L. S. (1988). *Toxicol. Appl. Pharmacol.* 93, 31-46. Octachlorodibenzo-*p*-dioxin (OCDD) is a ubiquitous environmental pollutant which has been reported to be nontoxic following acute exposure but has recently been shown to accumulate upon repeated exposure. To determine if this accumulation results in toxic effects, male Fischer 344 rats were treated with 50 µg/kg [<sup>14</sup>C]OCDD by gavage for 10, 20, 40, or 65 times (once a day, 5 days/week) and terminated 3 days postexposure. OCDD accumulated linearly with increasing number of doses and the liver was the major depot, while the adipose served as a secondary sink. Hepatic accumulation resulted in alteration of several biochemical parameters. In animals given 65 doses of OCDD, 7-ethoxyresorufin-*O*-deethylase activity was elevated 40-fold over controls. Total cytochrome *P*-450 content doubled and exhibited a 2-nm blue-shift in the Soret maximum for the CO-reduced complex. Treatment-related cytoplasmic fatty vacuolization in the liver was observed concomitant with the biochemical alterations. Thus, subchronic exposure to OCDD appears to cause effects similar to those observed following exposure to low levels of TCDD, but is only 1/100-1/1000 as potent. Such a potency, given the persistent environmental levels to which man may be exposed during a lifetime, suggests that OCDD may pose a potential risk to human health.