SITOX 2008 EUROTOX YOUNG SCIENTIST BEST POSTER AWARD FOR MULTI-NATIONAL COLLABORATIVE RESEARCH RESULTING FROM A COLLABORATION OF AT LEAST FOUR RESEARCHERS FROM DIFFERENT EUROPEAN COUNTRIES

Hepatic effects of a highly puri•ed PCB 180 in adult male and female Sprague–Dawley rats

Robert Roos 1,°Ø, Patrik Andersson2, Päivi Heikkinen3, Hans-Joachim Schmitz1, Leo van der Ven4, Satu Sankari5, Matti Viluksela 3, Dieter Schrenk1 1 *University of Kaiserslautern, Kaiserslautern, Germany, 2 University of Umea, Umea, Sweden,* 3 *University of Kuopio, Kuopio, Finland,* 4 *RIVM, Bilthoven, Netherlands* 5 *University of Helsinki, Helsinki, Finland*

PCB 180 is one of the most abundant PCBs found in food and environmental samples. Hepatotoxic and adaptive hepatic effects are considered critical for the risk assessment of PCBs. For investigation of the toxicity of non-dioxinlike (NDL)-PCBs such as PCB 180 the problem of contamination with dioxinlike (DL) constituents is of major importance. Rats were given by gavage over 28 days total doses of 3, 10, 30, 100, 300, 1000, or 1700mg/kg bw with a PCB 180 preparation containing 2.7 ng TEq/g PCB 180. No increase in serum ALAT or APHOS activitywas found, while liverweightwas increased at ≥300mg/kg in males and at 1700 mg/kg in females. Histopathological examination revealed centrilobular hepatocellular hypertrophy at >10 and >300 mg/kg bw in males and females, respectively. The hypertrophy was also most prominent in males, which further showed degenerative effects in hepatocytes at the highest dose (apoptosis, cytoplasmic inclusions). Furthermore, a significant increase in liver pentoxyresorufin *O*-dealkylase (PROD) was found in males at ≥10 mg/kg bw and in females at ≥30 mg/kg bw. In both genders, a significant induction of hepatic 7-ethoxyresorufin *O*-deethylase (EROD) activity was also observed. These findings suggest that, except for the top dose in males, PCB 180 does not exhibit overt hepatotoxicity within 28 days but leads to a variety of adaptive changes. The pattern of CYP induction indicates that PCB 180 acts as an agonist of the constitutive androstane receptor (CAR) andmay also have some agonistic activity at the Ah receptor.

doi:10.1016/j.toxlet.2008.06.671