

Guidelines/Criteria	
Reference:	Gyorkos J, Denomme MA, Leece B, Homonko K. 1985. Reconstituted halogenated hydrocarbon pesticide and pollutant mixtures found in human tissues: Effects on the immature male Wistar rat after short-term exposure. Can J Physiol Pharmacol 63(1):36-43.
In vivo Study Type Route of Administration Species & age of animals	Short-term rat study oral gavage immature male Wistar rats
Study Duration	6 days (dosed on days 1 and 3)
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	No Yes Similar Liver toxicity in general
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Liver weight and liver enzyme activities. Pathology in liver, thyroid, trachea, lungs, thymus, bronchial node and spleen. Depends on which endpoint
Individual Components Characterisation of individual compounds Name, exact chemical name, CAS no.	Three environmentally relevant mixtures. A mixture of 14 PCBs to approximate concentrations found in human milk samples, a mixture of 7 organochlorine pesticides to approximate the composition in human milk, and a mixture containing both the PCBs and the pesticides. The PCBs were 2,4,4'-trichlorobiphenyl, 2,2',5,5'-tetrachlorobiphenyl, 2,3',4,4'-tetrachlorobiphenyl, 2,2',4,5,5'-pentachlorobiphenyl, 2,3',4,4',5-pentachlorobiphenyl, 2,2',3,4',5,5'-hexachlorobiphenyl, 2,3,3',4,4'-pentachlorobiphenyl, 2,2',3,3',4,4'-hexachlorobiphenyl, 2,2',3,4,4',5'-hexachlorobiphenyl, 2,2',3,4',5,5',6-heptachlorobiphenyl, 2,2',3,4,4',5',6-heptachlorobiphenyl, 2,3,3',4,4',5-hexachlorobiphenyl, 2,2',3,4,4',5,5'-heptachlorobiphenyl, 2,2',3,3',4,4',5-heptachlorobiphenyl The organochlorine pesticides were DDT, HCB, HCH, dieldrin, heptachlor epoxide, trans-nanachlor and oxychlordane. Additional work was done with a mixture in which chlordane replaced trans-nanachlor and oxychlordane - results were very similar for both pesticide mixtures so they are considered together.
Were dose responses established for individual components? Were no effect levels established? Were doses below the NO(A)ELs investigated?	No No No
Mixtures Investigated Number of dose levels How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?) No. of technical replicates per exposure condition (<i>in vitro</i>) No. of animals per dose group (<i>in vivo</i>)	4, the lowest approximating the dose to a suckling infant over 180 days, and higher doses 2x, 10x and 100x this dose. Only simulated environmental mixtures were tested, and the composition was designed to simulate human breast milk.
Observations/Findings	For all three mixtures there was an increase in liver weight (big enough to be adverse) and mild histopathological changes in liver and thyroid at the 100x dose only. There was some liver enzyme induction at the 2x dose for the PCB and PCB + pesticides mixtures, and for all mixtures at 10x and 100x doses. Thyroid histopathology - mild alterations with architectural changes consisting of a reduction in follicle size and cytosolic changes including an increase in epithelial height with focal vacuolations. In the liver, nuclei exhibited marked variations in chromatin distribution with vesiculation of large nuclei and peripheralisation of chromatin to the membrane of prominent nucleoli; there was also a frequent appearance of pyknotic shrunken nuclei associated with increased eosinophilia of the nuclei (piecemeal necrosis); cytoplasmic changes were largely perivenous and midzone fine vacuolations and mild variations in volume which appeared to result from increased volume in the perivenous and midzone areas, possibly accompanied by mild reduction in volume in the periportal areas.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Good study of an environmental mixture. Dosing 6 months of contaminants to rats in two doses means that the exposures in the study were even more extreme in relation to human exposure than is stated in the report.