

Guidelines/Criteria	
Reference:	Crofton KM, Craft ES, Hedge JM, Gennings C, Simmons JE, Carchman RA, Carter Jr WH, DeVito MJ. 2005. Thyroid-hormone-disrupting chemicals: Evidence for dose-dependent additivity or synergism. Environ Health Perspect 113(11):1549-1554.
In vivo Study Type Route of Administration Species & age of animals	Gavage Female Long-Evans rats
Study Duration	4 days
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	No Yes Similar action assumed Thyroid toxicity
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Body weight, Thyroid (T4 levels using a standard radioimmunoassay kit, ED30) Hormone changes
Individual Components Characterisation of individual compounds Name, exact chemical name, CAS no. Were dose responses established for individual components? Were no effect levels established? Were doses below the NO(A)ELs investigated?	Yes TCDD, PCDD, TCDF, 1-PCDF, 4-PCDF, OCDF, PCB-28, PCB-52, PCB-77, PCB-101, PCB-105, PCB-118, PCB-126, PCB-138, PCB-153, PCB-156, PCB-169, PCB-180 No Yes Yes
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>)	TCDD 0.0001-10 µg/kg bw, PCDD 0.003 - 10 µg/kg bw, TCDF 0.3 - 100 µg/kg bw, 1-PCDF 0.03 - 100 µg/kg bw, 4-PCDF 0.03 - 90 µg/kg bw, OCDF 0.1 - 300 µg/kg bw, PCB-28 100 - 90000 µg/kg bw, PCB-52 100 - 90000 µg/kg bw, PCB-77 100 - 30000 µg/kg bw, PCB-101 50 - 30000 µg/kg bw, PCB-105 90 - 90000 µg/kg bw, PCB-118 10 - 10000 µg/kg bw, PCB-126 0.001 - 100 µg/kg bw, PCB-138 100 - 90000 µg/kg bw, PCB-153 100 - 90000 µg/kg bw, PCB-156 10 - 10000 µg/kg bw, PCB-169 1 - 1000 µg/kg bw, PCB-180 100 - 90000 µg/kg bw Highest mixture-dose levels of the individual chemicals were at or below their no observed effect levels Hormone levels were analysed in duplicates 4-14 rats / dose group
Observations/Findings	No deviation from additivity at the lowest dose, but greater-than-additive effect at the three highest mixture doses.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	