

| Guidelines/Criteria | |
|--|---|
| Reference: | Tofighi R, Johansson C, Goldoni M, Ibrahim WN, Gogvadze V, Mutti A, Ceccatelli S. 2011. Hippocampal neurons exposed to the environmental contaminants methylmercury and polychlorinated biphenyls undergo cell death via parallel activation of calpains and lysosomal proteases. <i>Neurotox Res</i> 19(1):183-94. |
| In vitro Study Type Route of Administration Species & age of animals | cytotoxicity in mouse hippocampal HT22 cells |
| Study Duration | 24 h |
| Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated? | yes dissimilar acting cell death (apoptosis vs. necrosis) |
| Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects <i>In vitro</i> | induction of apoptosis (staining with annexin V), cell necrosis (propidium iodide staining) |
| 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? | methylmercury, 3,3',4,4',5-pentachlorobiphenyl (PCB 126), 3,3',4,4',5,5'-hexachlorobiphenyl (PCB 153) 99.99%, no further purities given yes yes 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>) | 3 for MeHg, 2 for PCBs 1X NOEC MeHg & 1x NOEC PCB 126; 1x NOEC MeHg & 1x NOEC PCB153; 2X NOEC MeHg & 2x NOEC PCB 126; 2x NOEC MeHg & 2x NOEC PCB153; 4X NOEC MeHg & 2x NOEC PCB 126; 4x NOEC MeHg & 2x NOEC PCB153 |
| Observations/Findings | No effects were observed when combinations were tested at the individual NOECs. Increased apoptosis and increased necrosis was observed for individual compounds when tested at the corresponding 2xNOEC or higher concentrations and for the other combinations. |
| Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated) | Experiments on other parameters not including NOECs were not considered. Combinations of effective concentrations mainly pointed towards antagonistic effects, especially for necrosis. For the combination 4xNOEC MeHg & 2xNOEC PCB 153 a synergistic effect on apoptosis was proposed. |