**Gilbert et al, 2011**

| **Guidelines/Criteria** | |
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| Reference: | Gilbert KM, Rowley B, Gomez-Acevedo H, Blossom SJ. 2011. Coexposure to mercury increases immunotoxicity of trichloroethylene. Tox Sci 119(2):281-292. |
| ***In vivo*** **Study Type**<br>Route of Administration<br>Species & age of animals | Mouse liver and immunotoxicity study<br><br>Female autoimmune prone MRL +/+ mice, 8 weeks old |
| **Study Duration** | 8 weeks |
| **Type of Mixture**<br>Binary<br>>2 components<br>Similar acting or dissimilar<br>What Mode of Action was investigated? | <br>Yes<br>No<br>Dissimilar presumably<br>Immunotoxicity in general |
| **Parameters/End points Measured**<br>Target organs/Critical effects<br><br><br>Pharmacological changes or adverse effects | <br>Liver histopathology, weight gain and water consumption, splenic cellularity, cytokines, liver and brain gene expression and autoantibody production<br>In the absence of histopathology, the immunotox endpoints are probably not adverse. |
| **Individual Components**<br>Characterisation of individual compounds<br>Name, exact chemical name, CAS no.<br>Were dose responses established for individual components?<br>Were no effect levels established?<br><br><br><br><br>Were doses below the NO(A)ELs investigated? | <br><br>Trichlorothylene and mercury (as mercuric chloride)<br>Only two doses of TCE and one of mercury were tested<br>Questionable. All doses of single chemicals produced effects on one or more of the immune-related endpoints. They also increased liver histopathology score, but it was not stat sig, perhaps due to the relatively small group size for what seemed to be a very variable endpoint. Mercury and the high TCE dose decreased water consumption.<br>No |
| **Mixtures Investigated**<br>Number of dose levels<br><br><br><br>How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?)<br>No. of technical replicates per exposure condition (*in vitro*)<br>No. of animals per dose group (*in vivo*) | <br>2 of TCE, 1 of mercury. TCE was dosed at 9.9 or 187 mg/kg/day in drinking water, whilst mercuric chloride was dosed by sc injection twice a week at a dose equivalent to 0.26 mg/kg/day<br>No particular rationale.<br><br><br>6 mice per group |
| **Observations/Findings** | Significant reduction in water consumption for mercury alone, the higher TCE dose and for both mixture groups. All doses of single chemicals produced effects on one or more of the immune-related endpoints. They also increased liver histopathology score, but it was not statistically significant, perhaps due to the relatively small group size for what seemed to be a very variable endpoint. Significant increase in liver histopathology for both mixture groups, though the increase was only slightly higher than for single chemicals. |
| **Overall opinion**<br>(e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated) | <br>Valid study, though the histopathology was very variable. But the sporadic effects of single chemicals on various endpoint makes it hard to interpret. Arguably, without statistically significant histopathology, the other effects are not adverse. Therefore a NOAEL was achieved for single chemicals (but not a NOEL). |