Guidelines/Criteria	
Reference:	Merhi M, Demur C, Racaud-Sultan C, Bertrand J, Canlet C, Blas F, Estrada Y, Gamet‑Payrastre L. 2010. Gender-linked haematopoietic and metabolic disturbances induced by a pesticide mixture administered at low dose to mice. Toxicology 267:80-90.
In vivo **Study Type**	
Route of Administration	Oral gavage
Species & age of animals	Ten-week old female and male C57 BL/6J mice
Study Duration	Four weeks Pesticides administered three times per week for study duration.
Type of Mixture	
Binary	
>2 components	Yes. Six component mixture
Similar acting or dissimilar	Not clear, but expected to act on the haematopoietic system
What Mode of Action was investigated?	Impact of pesticides on the differentiation, proliferation and cell signalling pathways of haematopoietic cells.
Parameters/End points Measured	
Target organs/Critical effects	Organ weights (Liver, Spleen, Kidney); Metabonomics (1H-NMR on liver); Functional aspects and molecular mechanisms of haematopoiesis (included conventionalal haematological parameters)
Pharmacological changes or adverse effects	Adverse effects
Individual Components	
Characterisation of individual compounds	
Name, exact chemical name, CAS no.	Alachlor; Captan; Diazinon; Endosulfan; Mancozeb; Maneb
Were dose responses established for individual components?	No. Paper presented ADI and NOAEL values and target organs as taken from Monograph and Evaluation of Pesticides (JMPR 2005)
Were no effect levels established?	Not in these experiments. No effect levels taken from JMPR 2005.
Were doses below the NO(A)ELs investigated?	Not clear if NO(A)ELs stated in Table 1 are applicable to the endpoints considered in the current paper. Most likely, as they tested at ADIs.
Mixtures Investigated	
Number of dose levels	One
How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?)	Mixture level calculated from the ADIs extrapolated to mice on basis of mean bodyweight values. Alachlor - 0.01 µg Captan - 2 µg Diazinon - 0.004 µg Endosulfan - 0.12 µg Mancozeb - 1 µg Maneb - 1 µg
No. of technical replicates per exposure condition (*in vitro*)	not applicable
No. of animals per dose group (*in vivo*)	5 animals per group per sex.
Observations/Findings	Females - spleen weight increased Males - liver weight decreased Variations in hepatic metabolism mostly in male mice (in accordance with changes in liver weight) indicative of neoglucogenesis in males. Significant (non-pathological) changes to platelet count (30% increase, males); 8% decrease in red blood cell count; haemoglobin count and haematocrit (males); 1.4-fold increase in WBC (females; largely due to a 3-fold increase in polymorphonuclear neutrophiles) Sex-dependent deregulation of myeloid clonogenicity and differentiation (Colony Formation Units - Granulocyte Macrophage colonies more oriented to formation of granulocytes than macrophages in females, whereas the opposite in males).
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Could be considered as not relevant as the single substance dose-responses were not established in this study, but the NO(A)ELs are based on JMPR 2005 which consists of a robust data set. Clear effects from combination of doses not expected to result in effects individually. However, without good dose-response information on the single substances, it is not possible to determine if the observed combination effect is predictable using CA or IA.