

Guidelines/Criteria	
Reference:	Teramoto S, Saito R, Shirasu Y. 1980. Teratogenic effects of combined administration of ethylenethiourea and nitrite in mice. Teratology 21:71-78.
In vivo Study Type Route of Administration Species & age of animals	Developmental toxicity study Oral Pregnant female SLC-ICR mice
Study Duration	Single dose on day 6 or 8 or 10 or 12 of pregnancy, terminated on day 18
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes No ETU produces mutagens/teratogens by reaction with nitrite in stomach acid See above
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	Counts of implants, live and dead fetuses; weighed; gross abnormalities; skeletal examination; visceral abnormalities. Reduced foetal survival and various abnormalities
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?	Ethylenethiourea and sodium nitrite CAS numbers not given No - just a single dose of each tested, which was a NOEL Yes, 400 mg/kg for ETU and 200 mg/kg for NaNO ₂ Yes for NaNO ₂ only (50 and 100 mg/kg)
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>)	400 mg/kg of ETU in combination with 50/100/200 mg/kg NaNO ₂ NOEL or each, plus two lower doses of NaNO ₂ 9 to 18 dams
Observations/Findings	Increased foetal deaths, reduced foetal weight and variety of abnormalities in group with 400 mg/kg ETU and 200 mg/kg NaNO ₂ . No effect at the two lower doses of NaNO ₂ .
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Special case of chemical reaction between components of a mixture. Good study, but the proximity of the single component doses to the LOEL is unclear - though the authors cite an earlier experiment showing 800 mg/kg ETU is a NOEL. In a related experiment, the dosing of the two components was separated in time for the 400 mg/kg ETU & 200 mg/kg NaNO ₂ combination - when NaNO ₂ was dosed 2hrs after ETU there was no toxicity.