Guidelines/Criteria	
Reference:	Rider CV, Wilson VS, Howdeshell KL, Hotchkiss AK, Furr JR, Lambright CR, Gray LE Jr. 2009. Cumulative effects of in utero administration of mixtures of 'antiandrogens' on male rat reproductive development. Toxicol Pathol 37:100-113.
In vivo **Study Type** Route of Administration Species & age of animals	
Study Duration	
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects	
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?	
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 (*in vitro*) No. of animals per dose group (*in vivo*)	
Observations/Findings	This is a review of studies that were conducted by US EPA on mixtures of antiandrogens: * AR antagonists study with vinclozolin and procymidone (similar acting) * mixture study with pairs of phthalates (DBP+BBP and DEHP+DBP) (similar acting) * mixture studies with pesticides and phthalates with diverse modes of toxicity (linuron+BBP and procymidone+DBP) * seven compound mixture study (see Rider 2008) (dissimilar MoA) * ten chemical mixture study (see Rider 2010) (dissimilar MoA) All binary combinations in the binary mixture studies produced cumulative, dose-additive effects on the androgen dependent tissues. In addition, the more complex mixture studies with diverse modes of actions also behaved in a dose-additive manner (see also Rider 2008 and 2010). Their conclusion is that compounds (that disrupt development of the same reproductive tissues) acting by disparate mechanisms of toxicity display cumulative, dose-additive, effects when present in combination. Therefore the primary focus should be on the biological system rather than the mechanism of toxicity.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Not sure about experimental conditions as this is a review and does not describe a lot of details, e.g. were doses tested below NOAELs y/n etc. (although in the seven mixture study indeed doses below the individual NOAELs of the chemicals in the mixture were used, see Rider 2008 paper). However, they mention that they will increase the number of chemicals in the mixture to have all mixture components present in the mixture at doses clearly below their individual NOAELs - which will allow for greater distinction between models of response- and dose addition. The results of this study are described in the Rider 2010 paper.