

Guidelines/Criteria	
Reference:	Mondal S, Brankow DW, Heidelberger C. 1978. Enhancement of oncogenesis in C3H/10T1/2 mouse embryo cell cultures by saccharin. Science 201:1141-1142.
In vitro Study Type Route of Administration Species & age of animals	Mouse embryo cell culture transformation study
Study Duration	24hrs
Type of Mixture Binary >2 components Similar acting or dissimilar What Mode of Action was investigated?	Yes No Dissimilar and similar Pre-neoplastic cell transformation
Parameters/End points Measured Target organs/Critical effects Pharmacological changes or adverse effects <i>in vitro</i>	Number of transformed foci
Individual Components Characterisation of individual compounds Name, exact chemical name, CAS no.	TPA (12-O-tetradecanoyl-phorbol-13-acetate), pure saccharin, impure saccharin and MCA (3-methylcholanthrene)
Were dose responses established for individual components?	Not really dose-responses as only one or two doses were tested.
Were no effect levels established?	TPA, pure and impure saccharin all caused no effect at the single dose tested. MCA had a NOEL of 0.1 ug/ml (it caused an effect at 1 ug/ml).
Were doses below the NO(A)ELs investigated?	No
Mixtures Investigated Number of dose levels How does the mixture make-up compare to individual components? (e.g. low dose) equivalents used?)	5 relevant mixtures, all at a single dose. All relevant mixtures were tested at the NOEL of all components. In fact dosing was sequential, dosing either MCA or pure/impure saccharin first (as potential initiators) followed by either pure/impure saccharin or TPA second (as potential promoters).
No. of technical replicates per exposure condition (<i>in vitro</i>) No. of animals per dose group (<i>in vivo</i>)	32-50
Observations/Findings	Four of the five relevant mixtures caused transformation (MCA followed by TPA, MCA followed by pure saccharin, MCA followed by impure saccharin, and pure saccharin followed by TPA). Impure saccharin followed by TPA did not cause transformation.
Overall opinion (e.g. sufficient numbers of groups investigated, group sizes adequate, observations reproducible, low dose levels used investigated)	Seems well conducted. Without a better dose response interpretation is difficult.