

Adequate Dosing and the Maximum Tolerated Dose (MTD)

- “adequate high dose would generally be one that produces some toxic effects without unduly affecting mortality from effects other than cancer or producing significant adverse effects on the nutrition and health of the test animals.” (2005 U.S. EPA Guidelines)
- “The high dose would generally be considered inadequate if neither toxicity nor change in weight gain is observed.” (2005 U.S. EPA Guidelines)

Liver Pathology

- “Over the past 5 years, the practical meaning of the term *neoplastic nodule* has become synonymous with benign hepatocellular neoplasia or adenoma.” “Pathologists have become increasingly uncomfortable about including hepatoproliferative lesions that they believe to be hyperplasia rather than benign neoplasia under the term *neoplastic nodule*.” (Maronpot *et al.*, 1986)
- TDCPP Studies:
 - Significant increase in altered hepatocellular foci in female rats ($p < 0.05$)
 - Borderline increase in altered hepatocellular foci in males ($p = 0.07$).
- “...the terms *foci of cellular alteration*, *hepatocellular adenoma*, and *hepatocellular carcinoma* are believed to represent a spectrum of changes that comprise the natural history of neoplasia.” (Maronpot *et al.*, 1986)