

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.3800	Reproduction and fertility effects (rat)	Parental/Systemic NOAEL = 20 mg/kg/day LOAEL = 100 mg/kg/day (M/F), based upon increased liver weights in the P and F ₁ males and increased adrenal weights in the P females Offspring/Systemic NOAEL = 20 mg/kg/day LOAEL = 100 mg/kg/day (M/F), based upon pup mortality Reproductive NOAEL = 100 mg/kg/day LOAEL = not determined
870.4300	Combined chronic toxicity/carcinogenicity rodents (rat)	NOAEL = 64 mg/kg/day (M/F) LOAEL = not determined Equivocal evidence of carcinogenicity
870.4300	2-Year feed/carcinogenic (rat)	NOAEL = 1.83/2.07 mg/kg/day (M/F) LOAEL = 187/216 (M/F), based upon effects on the incisors including abnormal amelogenesis No evidence of carcinogenicity
870.4100	Chronic toxicity nonrodents (dog)	NOAEL = 4.62/4.79 mg/kg/day (M/F) LOAEL = 23.5/23.8 mg/kg/day (M/F), based upon increased alkaline phosphatase activity, increased liver weights, liver enlargement (females), and incidences of centrilobular hepatocellular swelling in the liver
	78-Week carcinogenic mouse	NOAEL = 242/243 (M/F) LOAEL = 484/482 (M/F), based on a slight increase in the incidence of a fatty change in the centrilobular hepatocytes in males
870.4200	Carcinogenicity mouse	NOAEL = 241/243 mg/kg/day (M/F) LOAEL = not determined No evidence of carcinogenicity
Non-guideline	13-Week study: Effect on proliferative activity of testicular interstitial cells in rat	A toxic level of the test substance did not affect the proliferative activity of testicular interstitial cells
870.5100	Gene mutation - reverse gene mutation assay in bacteria	When tested up to cytotoxic levels, there was no evidence of induced mutant colonies over background
Non-guideline	Gene mutation - reverse gene mutation assay in bacteria	When tested up to cytotoxic levels, there was no evidence of induced mutant colonies over background
870.5300	Gene mutation - <i>in vitro</i> forward gene mutation assay in mouse lymphoma cells	When tested up to cytotoxic levels, mutagenic in the presence of S9 activation and equivocal for mutagenicity in the absence of S9 activation
870.5375	Cytogenetics - <i>in vitro</i> mammalian cytogenetics assay	When tested up to cytotoxic levels, not clastogenic in the presence or absence of S9 activation
870.5395	Bone marrow micronucleus assay	There was no significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any treatment time
870.5550	Unscheduled DNA synthesis (UDS) in primary rat hepatocytes/mammalian cell cultures	When tested up to cytotoxic levels, there was no evidence that UDS was induced by the test substance

B. Toxicological Endpoints

The dose at which the NOAEL from the toxicology study identified as appropriate for use in risk assessment is used to estimate the toxicological level of concern (LOC). However, the LOAEL is sometimes used for risk assessment if

no NOAEL was achieved in the toxicology study selected. An uncertainty factor (UF) is applied to reflect uncertainties inherent in the extrapolation from laboratory animal data to humans and in the variations in sensitivity among members of the

human population as well as other unknowns. An UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intraspecies differences.

For dietary risk assessment (other than cancer) the Agency uses the UF to