

TABLE 2.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline number	Study Type	Results
870.3800	2-Generation reproduction and fertility effects	Parental/systemic NOAEL = 30 ppm (2.4/2.5 mg/kg/day M/F) Parental/systemic LOAEL = 300 ppm (23.8/25.2 mg/kg/day M/F), based on decreased body weights and food consumption and on increased incidences of bile duct hyperplasia and liver necrosis in males and females of both generations Offspring NOAEL = 300 ppm (23.8/25.2 mg/kg/day M/F) Offspring LOAEL = 1,000 ppm (79.6/83.8 M/F), based on decreased pup body weight and body weight gain in both generations Reproductive NOAEL = 30 ppm (2.4/2.5 mg/kg/day M/F) Reproductive LOAEL = 300 ppm (23.8/25.2 mg/kg/day M/F) based on an increase in the number of days to mating in both generations
870.4100	1-Year chronic oral (capsule) toxicity (dog)	NOAEL = 500 mg/kg/day M/F LOAEL = 1,000 mg/kg/day M/F, based on decreased body weight gain in males, decreased MCV, MCH, and mean corpuscular hemoglobin concentration (MCHC); increased thrombocytes and red cell volume distribution width; hepatic histopathology: glycogen disposition, inclusion bodies in cytoplasm, and pigment disposition in both sexes, and focal vacuolation in females
870.4200	18-Month carcinogenicity dietary study (mouse)	NOAEL = 10 ppm (1.17/1.20 mg/kg/day M/F) LOAEL = 60 ppm (6.96/6.59 mg/kg/day M/F), based on enlarged livers with increased weights, and hepatic microscopic lesions including Kupffer cell hyperplasia, inflammatory cell infiltration, and single cell necrosis in both sexes and on deposits of lipofuscin in males No evidence of carcinogenicity
870.4300	Combined 2-Year chronic/carcinogenicity dietary study (rat)	NOAEL = 100 ppm (3.76/4.43 mg/kg/day M/F) LOAEL = 300 ppm (11.4/13.0 mg/kg/day M/F), based on minimal hepatic abnormalities in the females, including a fatty change and increased mitotic activity No evidence of carcinogenicity
870.5100	<i>In vitro</i> bacterial gene mutation	Negative in a reverse gene mutation assay in strains TA98, TA100, TA102, TA1535, TA1537 of <i>S. typhimurium</i> and strain WP2(uvrA) of <i>E. coli</i> in the presence and absence of mammalian metabolic activation
870.5300	<i>In vitro</i> mammalian cells in culture	Evidence of borderline induction of mutant colonies in presence of S9 in a mammalian cell gene mutation assay at the hypoxanthine guanine phosphoribosyl transferase (HGPRT) locus of Chinese hamster V79 cells
870.5375	<i>In vitro</i> mammalian cytogenetics	Negative. No evidence of increase in chromosome aberrations over background
870.5395	<i>In vivo</i> mammalian cytogenetics - micronucleus assay (mouse)	Negative. No increase in frequency of micronucleated polychromatic erythrocytes
870.5550	Other genotoxicity - unscheduled DNA synthesis (UDS)- <i>in vivo/in vitro</i>	Negative. No evidence of induction of UDS; no indications of induction of DNA damage
870.5550	Other genotoxicity - UDS - <i>in vitro</i>	Negative. No evidence of induction of UDS; no indications of induction of DNA damage in primary rat hepatocytes in culture
870.6200	Acute neurotoxicity screening battery (rat)	NOAEL = 2,000 mg/kg LOAEL = Not determined No evidence of neurotoxicity
870.6200	Subchronic neurotoxicity screening battery (rat)	NOAEL = 300 ppm 21/24 mg/kg/day M/F LOAEL = 1,000 ppm 72/76 mg/kg/day M/F, based on liver histopathology and decreased motor activity at week 13 in the males No evidence of neurotoxicity