

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

Guideline No.	Study Type	MRID No. (year)/Classification/Doses	Results
870.4100	Chronic toxicity dog	43492834 (1994) Acceptable/guideline 0, 60, 120, 240 ppm M: 0, 2.1, 4.0, 8.7 mg/kg/day F: 0, 2.3, 4.5, 10.1 mg/kg/day	NOAEL = 4.0/4.5 mg/kg/day, M/F LOAEL = 8.7/10.1 mg/kg/day, M/F, based on decreased body weight/body weight gains
870.4200	Carcinogenicity mouse	43492838 (1994) Acceptable/guideline 0, 20, 120, 240 ppm M: 0, 2.8, 16.6, 34.5 mg/kg/day F: 0, 3.7, 21.9, 44.5 mg/kg/day	NOAEL = 2.8/3.7 mg/kg/day, M/F LOAEL = 16.6/21.9 mg/kg/day, M/F, based on decreased body weight gains, brain vacuolation, and scabbing of the skin (males) No evidence of carcinogenicity
870.4300	Combined chronic/carcinogenicity in rat	43492837 (1994) Acceptable/guideline 0, 60, 300, 600 ppm M: 0, 2.9, 15.0, 30.8 mg/kg/day F: 0, 3.6, 18.6, 37 mg/kg/day	NOAEL = 15 mg/kg/day, males LOAEL = 30.8 mg/kg/day, males, based on anemia NOAEL = 3.6 mg/kg/day, females LOAEL = 18.6 mg/kg/day, females, based on decreased body weight/body weight gain Classification: "Suggestive Evidence of Carcinogenicity, but Not Sufficient to Assess Human Carcinogenic Potential" based on significant trends in liver tumors (adenomas and combined adenomas/carcinomas), malignant histiocytic sarcomas, and testicular cell tumors in male rats and uterine polyps in female rats seen at the highest dose
870.5100	Bacterial reverse mutation	42770223 (1993) Acceptable/Guideline	Negative for reverse mutation in <i>S. typhimurium</i> strains TA 98, TA 100, TA 1535, TA 1537, TA 1538 and <i>E. coli</i> strain WP2 uvrA- exposed up to cytotoxicity (50 µg/plate, +/- S9)
870.5300	<i>In vitro</i> mammalian cell gene mutation in Chinese hamster ovary cells (CHO/HGPRT)	42770224, 43187601 (1993) Acceptable/Guideline	Independently performed tests were negative up to a cytotoxic and precipitating concentration (500 µg/ml) in the presence of S9 activation or the solubility limit (250 µg/ml) without S9 activation
870.5375	<i>In vitro</i> mammalian chromosome aberration (CHO)	43492843 (1994) Acceptable	The test was negative up to 100 µg/ml -S9 or 25 µg/ml +S9; higher doses with or without S9 activation were cytotoxic
870.5385	<i>In vitro</i> chromosome aberration assay in Chinese hamster lung (CHL) cells	43492839 (1994) Acceptable/Guideline	The test was negative up to a precipitating level without S9 activation (225 µg/ml) or a concentration range of 3.5–14.1 µg/ml +S9. Higher S9-activated doses (≥28 µg/ml) were cytotoxic
870.5395	Mammalian micronucleus (mouse)	42770225, 43187602 (1993, 1994) Acceptable/Guideline	The test was negative in mice administered single oral gavage doses of 7.5–30 mg/kg (males) or 5–20 mg/kg (females). Clinical toxicity (deaths in males and diarrhea in females) was seen at the HDT. There was, however, no evidence of cytotoxicity for the target organ
870.5550	Unscheduled DNA synthesis	42770226 (1993) Acceptable/Guideline	Negative for inducing unscheduled DNA synthesis in primary rat hepatocyte cultures exposed up to severely toxic concentrations (≥30 µg/ml)
870.6200	Acute neurotoxicity screening battery rat	43492829 (1994) Acceptable/guideline 0, 45, 90, 180 mg/kg	NOAEL = 45 mg/kg/day LOAEL = 90 mg/kg/day, based on lethargy in male rats on the day of treatment
870.6200	Chronic neurotoxicity rat	43492833 (1994) Acceptable/Guideline 0, 60, 300, 600 ppm M: 0, 2.6, 13.6, 28.2 mg/kg/day F: 0, 3.4, 18, 37.4 mg/kg/day	NOAEL = 2.6/3.4 mg/kg/day, M/F LOAEL = 13.6/18 mg/kg/day, M/F, based on the presence of myelinopathic alterations in the central nervous system (CNS) in male rats and decreased average body weights/body weight gains, food efficiency, absolute food consumption (females) and water consumption (males)