

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

Guideline No.	Study Type	Results
870.3800	Reproduction and fertility effects (rats)	Parental/Systemic NOAEL = M/F: 11.3/14.2 mg/kg/day LOAEL = M/F: 44.7/53.3 mg/kg/day based on decreased body weight, body weight gain, and food consumption; and hepatotoxicity in the liver. Reproductive NOAEL = M/F: 44.7/53.3 mg/kg/day LOAEL = M/F: none (>44.7/53.3 mg/kg/day) Offspring NOAEL = M/F: 11.3/14.2 mg/kg/day LOAEL = M/F: 44.7/53.3 mg/kg/day based on decreased body weights for F ₁ and F ₂ pups throughout lactation.
870.4100	Chronic toxicity in dogs	NOAEL = M: 1.2 mg/kg/day. F: 1.2 mg/kg/day. LOAEL = M: 8.8 mg/kg/day based on lens cataracts in eyes. F: 9.3 mg/kg/day based on lens cataracts in eyes. No other adverse effects were observed in M or F.
870.4100	Chronic toxicity in Cynomolgus monkeys	NOAEL = M: 100 mg/kg/day. F: 100 mg/kg/day. LOAEL = M: 1,000 mg/kg/day based on mild hemolytic anemia with secondary responses in spleen, liver and kidney; and sinus dilatation in spleen. F: 1,000 mg/kg/day based on mild hemolytic anemia with secondary responses in spleen, liver and kidney; and sinus dilatation in spleen. No evidence of lens cataracts in eyes of M or F.
870.4200	Carcino-genicity in mice	NOAEL = M: 96 mg/kg/day. F: 130 mg/kg/day. LOAEL = M: 274 mg/kg/day based on slight hepatotoxicity in the liver; no anemia. F: 392 mg/kg/day based on amyloidosis and slight hepatotoxicity in the liver; no anemia. No evidence of carcinogenicity in M or F.
870.4300	Combined chronic toxicity/carcinogenicity in rats	NOAEL = M: 8.4 mg/kg/day. F: 2.2 mg/kg/day LOAEL = M: 16.8 mg/kg/day based on slight hemolytic anemia with compensatory erythropoiesis and secondary responses in spleen and bone marrow; and mild hepatotoxicity in the liver. F: 10.7 mg/kg/day based on decreased body weight gain and slight hemolytic anemia. At 23.0 mg/kg/day, also secondary responses to anemia in spleen, bone marrow and/or liver; and mild hepatotoxicity in the liver. No evidence of carcinogenicity M or F.
870.5100	Reverse gene mutation	Negative without and with S-9 activation up to limit dose of 5,000 µgram(g)/plate.
870.5300	Forward gene mutation (<i>In Vitro Mammalian Cell Gene Mutation Test</i>)	Negative without and with S-9 activation up to the limit of solubility (in DMSO) of 30 µg/mL.
870.5300	Forward gene mutation (CHO/HGPRT locus)	Negative without and with S-9 activation up to cytotoxic concentrations (≥ 200 µg/mL without S-9 and ≥ 150 µg/mL with S-9).
870.5375	Chromosome aberration (human lymphocytes)	Positive (weak clastogenic effect) without S-9 activation. Statistically significant increases in percentage of aberrant cells at several dose levels ranging from 5–15 µg/mL. Cytotoxicity was observed at 10–18 µg/mL. Negative with S-9 activation.
870.5375	Chromosome aberration (human lymphocytes)	Positive (weak clastogenic effect) without S-9 activation. Statistically significant increases in percentage of aberrant cells at several dose levels ranging from 15–30 µg/mL. Cytotoxicity was observed at 20–30 µg/mL. Negative with S-9 activation.
870.5395	Micronucleus assay (mouse bone marrow)	Negative at single-oral doses of up to limit dose of 5,000 mg/kg.
870.5550	Unscheduled DNA synthesis (rat hepatocytes)	Positive response (increased net nuclear grain counts) observed at several treatment levels ranging from 0.05–10 µg/mL. Cytotoxicity was observed at 10 µg/mL.
870.5550	Unscheduled DNA synthesis (rat hepatocytes)	Negative at treatment levels up to 10 µg/mL. Cytotoxicity was observed at 10 µg/mL.
870.5550	Unscheduled DNA synthesis (prim. rat hepatocytes)	Negative at treatment levels up to 5.0 µg/mL. Cytotoxicity was observed at 2.5 and 5.0 µg/mL.
870.5550	Unscheduled DNA synthesis (hepatocytes derived from male rats given Famoxadone)	Negative at single-oral doses of up to 2,000 mg/kg. No marked increases in net nuclear grain counts or percentage of cells in repair in hepatocyte cultures.