

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

| Guideline No. | Study Type | Results |
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| 870.3700 | Prenatal developmental in rodents (rat) | Maternal NOAEL = 25 mg/kg/day Maternal LOAEL = 75 mg/kg/day, based upon reduced body weight, body weight change and food consumption Developmental NOAEL = 10 mg/kg/day Developmental LOAEL = 25 mg/kg/day, based upon significant increase in overall malformations, and generalized dose-related delay in skeletal ossification; at 75 and 150 mg/kg/day significant decrease in fetal body weights; at 150 mg/kg/day increased early resorptions resulting in reduced litter size. |
| 870.3700 | Prenatal developmental in nonrodents (rabbit) | Maternal NOAEL 32 mg/kg/day Maternal LOAEL was not established Developmental NOAEL = 4 mg/kg/day Developmental LOAEL = 8 mg/kg/day, based upon an increase in skeletal anomalies of the cervical and thoracic vertebrae and ribs; at 32 mg/kg/day, cleft palate was also observed. |
| 870.3800 | 2-Generation reproduction and fertility effects (rat) | Systemic toxicity NOAEL = 6.5 males and 7.9 females mg/kg/day Systemic toxicity LOAEL = 32.1 males and 40.6 females mg/kg/day, based on reduced pre-mating body weight, body weight gain, and food consumption for P males; and decreased gestation and lactation body weight for F1 females Reproductive toxicity NOAEL 97.9 mg/kg/day for males and 130 mg/kg/day for females. Reproductive toxicity LOAEL was not established Offspring toxicity NOAEL = 6.5 males and 7.9 females mg/kg/day Offspring toxicity LOAEL = 32.1 female and 40.6 females mg/kg/day, based upon decreased F1 pup viability on postnatal days 0–4 and on a significant reduction in F2b pup weight. |
| 870.4100 | Chronic toxicity (dog) | Systemic toxicity NOAEL = 3.0/3.1 mg/kg/day for males/ and females Systemic toxicity LOAEL = 5.7 mg/kg/day (HDT in males), based upon depressed weight gains through week 12 and changes in the hematology and blood chemistry in males LOAEL was not established for females. |
| 870.4300 | Combined chronic toxicity/ carcinogenicity rodents (rat) | Systemic toxicity NOAEL = 4.08 mg/kg/day for males and 5.36 mg/kg/day for females Systemic toxicity LOAEL = 30.3 mg/kg/day for males and 38.4 mg/kg/day for females, based upon decreased body weight, body weight gain, and food efficiency, increased incidence of elongate spermatid degeneration and increased aggressiveness and/or hyperactivity in males and increased incidence of non-neoplastic lesions of the lungs, liver, sciatic nerve and retinal atrophy in females No evidence of carcinogenicity. |
| 870.4200 | Carcinogenicity mice | Systemic toxicity NOAEL = 4.19 mg/kg/day for males and 5.83 mg/kg/day for females, lowest dose tested (LDT) Systemic toxicity LOAEL = 42 mg/kg/day for males and 58.1 mg/kg/day for females HDT, based upon increased frequency of sperm cyst/cystic dilatation, tubular dilatation and lymphoid aggregates in males and hyperplastic gastropathy in females No evidence of carcinogenicity. |
| 870.5100 | Gene mutation | Cytotoxicity in all strains was seen at 750 µg/plate -S9 and 1,000 µg/plate +S9. The positive controls induced the expected mutagenic responses in the appropriate tester strain. There was, however, no evidence that the test material induced a mutagenic effect under any test condition. |
| 870.5300 | <i>In vitro</i> mammalian cell gene mutation assay (CHO) | Severe cytotoxicity was seen at 750 µg/mL -S9 and 1,000 µg/mL +S9. The positive controls induced the expected mutagenic responses. There was, however, no evidence that the test material was mutagenic at the Hypoxanthine Guanine Phosphoribosyl Transferase locus at any dose under any assay condition. |
| 870.6200 | Subchronic neurotoxicity screening battery (rat) | No effects on the functional observation battery, or motor activity were observed. No treatment-related gross or microscopic findings in the nervous system or skeletal muscles of the male and female rats were observed The neurotoxicity NOAEL 3,000 ppm (224 mg/kg/day in males and 333 mg/kg/day in females; HDT). Neurotoxicity LOAEL was not established. |