

TABLE 1A.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY FOR METOLACHLOR (PC CODE 108801)—Continued

| Guideline No. | Study Type | Results |
|---------------|--|--|
| 870.3800 | Reproduction and fertility effects | <p>Parental Toxicity NOAEL = 75.8 mg/kg/day (F₀ males/females: 75.8/85.7 mg/kg/day; F₁ males/females: 76.6/84.5 mg/kg/day).</p> <p>Parental LOAEL was not established</p> <p>Reproductive toxicity NOAEL = 75.8 mg/kg/day (F₀ males/females: 75.8/85.7 mg/kg/day; F₁ males/females: 76.6/84.5 mg/kg/day).</p> <p>Reproductive toxicity LOAEL was not established</p> <p>Offspring NOAEL = 23.5 mg/kg/day (F₀ males/females: 23.5/ 26.0 mg/kg/day; F₁ males/females: 23.7/25.7 mg/kg/day)</p> <p>Offspring LOAEL = 75.8 mg/kg/day based on F₀ males/females: 75.8/85.7 mg/kg/day; F₁ males/females: 76.6/84.5 mg/kg/day) based on decreased body weight.</p> |
| 870.4100 | Chronic toxicity dogs | <p>NOAEL = 9.7 mg/kg/day for females</p> <p>LOAEL = 33mg/kg/day for females based on decreased body weight</p> <p>NOAEL =32.7 mg/kg/day for males.</p> <p>LOAEL for males was not established</p> |
| 870.4300 | Chronic Toxicity/Carcinogenicity in Rodents | <p>NOAEL = 15 mg/kg/day for females</p> <p>LOAEL = 150 mg/kg/day for females based on slightly decreased body weight gain and food consumption.</p> <p>The NOAEL =150 mg/kg/day for males.</p> <p>The LOAEL was not established for males.</p> <p>Administration of doses up to 3,000 ppm (150 mg/kg/day) was associated with statistically significant increases in liver adenomas and combined adenoma/carcinoma in female rats. In male rats, there was a statistically significant trend but not pair-wise significance for liver tumors.</p> |
| 870.4300 | Carcinogenicity mice | <p>NOAEL = 150 mg/kg/day</p> <p>LOAEL = 450 mg/kg/day based on possible treatment-related deaths in females and decreased body weight/body weight gain in males and females</p> <p>no evidence of carcinogenicity</p> |
| 870.5100 | Gene mutation -bacterial reverse mutation | negative up to cytotoxic doses (1,000 µg/plate) |
| 870.5300 | Gene mutation - mouse lymphoma | no effect on the incidence of mutations in the presence or absence of metabolic activation |
| 870.5395 | Cytogenetics Micro-nucleus assey in Chinese hamsters | no effect of treatment on incidence of micronuclei induction |
| 870.5450 | Cytogenetics dominant lethal assey in mice | no effect on embryonic death, pre- and post-implantation or fertility rates in mated females |
| 870.5550 | Other Effects DNA Damage/Repair in rat hepatocytes | negative |
| 870.5550 | Other Effects DNA Damage/Repair in human fibroblasts | negative |
| 870.5550 | Other Effects Unscheduled DNA synthesis in rat hepatocytes | negative for induction of UDS; however, significant increases in percentage of cells in S-phase were observed in females dosed at 500 mg/kg (but not at 1,000 or 1,500 mg/kg) and sacrificed at 15 hours |
| 870.7485 | Metabolism and pharmacokinetics Unacceptable | <p>The major metabolic pathway proposed from analysis of urinary as well as fecal metabolites is one of cleavage of the ether bond and subsequent oxidation to the carboxylic acid, as well as hydrolytic removal of the chlorine atom. Conjugation of CGA 24705 or metabolites with gluronic acid or sulfate does not appear to occur.</p> <p>Aqueous extractable urinary radioactivity contained 58% of the total urinary radioactivity and was composed of 5 different radioactive fractions, which were not identified.</p> <p>Current guideline recommendations as to dose levels and use of both sexes in metabolism studies were not followed. Thus, whether the metabolic pattern is altered with dose or repeated exposure cannot be evaluated from these data.</p> |