

TABLE 1.—TOXICITY PROFILE OF PYRIPROXYFEN TECHNICAL—Continued

Guideline No./Study Type	MRID No. (year)/ Classification /Doses	Results
870.4100b Chronic toxicity—dogs	42178309 (1991) Acceptable/ guideline 0, 30, 100, 300, or 1,000 mg/kg/day	NOAEL = 100 mg/kg/day (M) and (F) LOAEL = 300 mg/kg/day (M), 300 mg/kg/day (F) based on decreased body weight gain and increased relative liver weight (both sexes) and increased cholesterol and triglycerides and decreased red cell counts and hemoglobin in males
870.4300 Chronic/Carcinogenicity— rats	42178314, 43210501, 43210502, 43210503 (1991) Acceptable/ guideline 0, 120, 600, or 3,000 ppm M: 0, 5.42, 27.31, or 138.0 mg/kg/ day F: 0, 7.04, 35.1, or 182.7 mg/kg/day	NOAEL = 138 mg/kg/day (M), 35.1 mg/kg/day (F) LOAEL = not established in males, 182.7 mg/kg/day (F) based on decreases in body weight gain No evidence of carcinogenicity
870.4200 Carcinogenicity—mice	42178310 (1991) Acceptable/ guideline 0, 120, 600, or 3,000 ppm M: 0, 16.8, 84.0, or 420 mg/kg/day F: 0, 21.9, 109.5, or 547 mg/kg/day	NOAEL = 84 mg/kg/day (M), 109.5 mg/kg/day (F) LOAEL = 420 mg/kg/day (M), 547 mg/kg/day (F) based on renal lesions (M) and (F) No evidence of carcinogenicity
870.5265 Gene mutation	44503506 (1995) Acceptable/ guideline	Non-mutagenic when tested up to 5,000 micrograms (mg)/plate or cytotoxic levels, in presence and absence of activation; in <i>S. typhimurium</i> strains TA98, TA100, TA1535, and TA1537; and in <i>E.coli</i> strain WP2uvra with 2-OH-PY (metabolite of pyriproxyfen).
870.5265 Gene mutation	44503507 (1993) Acceptable/ guideline	Non-mutagenic when tested up to 5,000 mg/plate or cytotoxic levels, in presence and absence of activation; in <i>S. typhimurium</i> strains TA98, TA100, TA1535, and TA1537; and in <i>E.coli</i> strain WP2uvra with 4'—OH-PY, 5'—OH-PYR, DPH-PYR, POPA, and PYPAC (metabolites of pyriproxyfen).
870.5265 Gene mutation	44503508 (1995) Acceptable/ guideline	Non-mutagenic when tested up to 5,000 mg/plate or cytotoxic levels, in presence and absence of activation; in <i>S. typhimurium</i> strains TA98, TA100, TA1535, and TA1537; and in <i>E.coli</i> strain WP2uvra with 2,5-OH-PY (metabolite of pyriproxyfen).
870.5265 Gene mutation	42178315 (1988) Acceptable/ guideline	Non-mutagenic when tested up to 5,000 mg/plate or cytotoxic levels, in presence and absence of activation; in <i>S. typhimurium</i> strains TA98, TA100, TA1535, TA1537, and TA1538; and in <i>E.coli</i> strain WP2uvra with 2-OH-PY (pyriproxyfen technical).
870.5300 Gene mutation	42178316 (1990) Acceptable/ guideline	Non-mutagenic at the HGPRT locus in Chinese hamster lung V79 cells tested up to cytotoxic concentrations or limit of solubility, in presence and absence of activation.
870.5375 Chromosome aberration	41321722 (1989) Acceptable/ guideline	Did not induce structural chromosome aberration in Chinese hamster ovary (CHO) cell cultures in the absence or presence of activation.
870.5550 Unscheduled DNA synthesis	42178317 (1988) Acceptable/ guideline	There was no evidence that unscheduled DNA synthesis, as determined by radioactive tracer procedures (nuclear silver grain counts) was induced in HeLa cells exposed up to cytotoxic levels, both in the presence or absence of S-9.
870.7485Metabolism and pharmacokinetics— rat	42178318 (1988) Acceptable/ guideline	Rats were orally dosed with ¹⁴ C-labeled pyriproxyfen at 2 or 1,000 mg/kg and at repeated oral doses (14 daily doses) of unlabeled pyriproxyfen at 2 mg/kg followed by administration of a single oral dose of labeled pyriproxyfen at 2 mg/kg. Most radioactivity was excreted in the feces (81–92%) and urine (5–12%) over a 7 day collection period. Expired air containing CO ₂ was not detected. Tissue radioactivity levels were very low (less than 0.3%) except for fat. Examination of urine, feces, liver, kidney, bile, and blood metabolites yielded numerous (> 20) identified metabolites when compared to synthetic standards. The major biotransformation reactions of pyriproxyfen include: 1. Oxidation of the 4'— position of the terminal phenyl group. 2. Oxidation at the 5'—position of pyridine. 3. Cleavage of the ether linkage and conjugation of the resultant phenols with sulfuric acid.