

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

Guideline No.	Study Type	Results
870.5300	Gene mutation	<p>In mammalian cell gene mutation assays at the TK locus, L5178Y mouse lymphoma cells cultured <i>in vitro</i> were exposed to pyraflufen-ethyl in dimethylsulfoxide (DMOS) in the absence of mammalian metabolic activation (S9-mix) and with S9-mix. Concentrations 160 µg/mL were insoluble; cytotoxicity was seen at 80 µg/mL -S9 and 160 µg/mL +S9. There was no increase in the number of mutant colonies over background in the absence of S9-mix but a non-reproducible dose-related increase in the number of mutant colonies was seen in the presence of S9-mix.</p> <p>In mammalian cell gene mutation assays at the TK locus, L5178Y mouse lymphoma cells cultured <i>in vitro</i> were exposed to pyraflufen-ethyl in DMSO in the absence of mammalian metabolic activation (S9-mix) and with S9-mix. There was no evidence of induced mutant colonies over background up to cytotoxic concentrations (50 µg/mL-S9; and 350 µg/mL +S9).</p>
870.5375	Chromosomal aberration	<p>In a mammalian cell cytogenetics assay, human primary lymphocyte cultures were exposed to pyraflufen-ethyl in DMSO without metabolic activation (S9-mix) or with S9-mix. Compound precipitation occurred at 2,600 µg/mL +/- S9. There was no evidence of chromosomal aberration induction over background.</p>
870.5395	Cytogenetics	<p>In a CD-1 mouse bone marrow micronucleus assay, five mice/sex/dose/harvest time were treated via oral gavage with pyraflufen-ethyl in corn oil. ET-751 was tested to the limit (LTD) dose of 5,000 mg/kg bwt. Signs of compound toxicity were limited to piloerection, hunched posture in one female, and piloerection and hunched posture in one male receiving 5,000 mg/kg. No bone marrow cytotoxicity was seen at any dose. There was no statistically significant increase in the frequency of micronucleated polychromatic erythrocytes in bone marrow after any dose or treatment time.</p>
870.5500	Bacillus subtilis	<p>In a differential killing/growth inhibition assay in bacteria, strains H17 (rec+) and M45 (rec-) of <i>B. subtilis</i> were exposed to pyraflufen-ethyl in DMSO in the presence and absence of metabolic activation (S9-mix). There was no evidence of greater growth inhibition or cell killing in repair-defective strains compared to repair competent strains up to the limit of test material solubility.</p>
870.5550	Unscheduled DNA synthesis (UDS)	<p>In an <i>in vivo/in vitro</i> UDS assay in rat hepatocytes, pyraflufen-ethyl was administered to five SPF outbred albino Hsd/Ola Sprague-Dawley male rats per test group by oral gavage (four of the five rats were used for hepatocyte culture). No signs of overt toxicity to the test animals or cytotoxic effects to the target cells were seen up to the LTD (2,000 mg/kg). The mean net nuclear grain count was below zero for both doses at both treatment times indicating no induction of UDS as tested in this study.</p>