

considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The nature of the toxic effects caused by quinoxifen are discussed below and summarized in Table 1 of this unit as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies reviewed.

The primary target organs affected by quinoxifen are the liver and kidney. Liver effects were seen in rat and mouse subchronic and dog chronic studies. Subchronic effects in rats and mice included increased liver weights, hepatocellular hypertrophy and individual cell hepatocellular necrosis. These effects were noted at high doses and not observed in the chronic rat and mouse studies since they were

performed at lower doses. Chronic effects in the dog included increased liver weights, increased alkaline phosphatase levels and increased incidences of slight microscopic hepatic lesions (increased bile in canaliculi and increased hepatocyte size). Kidney effects were noted only in the rat combined chronic/carcinogenicity study which resulted in an increased severity of chronic progressive glomerulonephropathy in the males. Rabbits were much more susceptible to the effects of quinoxifen than any other species. Systemic effects observed in the rabbit developmental study included inanition, loss of body weight, perineal soiling, blood in the cage pan associated with urine, and abortions. Body weight decrements were noted in the rat and/or mouse subchronic, chronic and carcinogenicity studies and the rabbit developmental and rat reproduction

studies. No effects were noted via the dermal route. No evidence of neurotoxicity or neuropathology was seen in any of the submitted studies, including the acute and subchronic neurotoxicity studies. There was no evidence of carcinogenic potential in either the rat chronic toxicity/carcinogenicity or mouse carcinogenicity studies and no concern for mutagenicity. There was no evidence of increased susceptibility in the oral rat or rabbit developmental studies. There was an increased quantitative susceptibility of young animals following pre/postnatal exposure to rats in the reproduction study. In this study, no maternal effects were observed up to the highest dose tested (100 milligrams/kilograms/day (mg/kg/day)); however, minimally reduced  $F_{1a}$  pup weights were noted at 100 mg/kg/day.

TABLE 1.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY

Guideline No.	Study Type	Results
870.3100	90-Day oral toxicity rodents (rat)	NOAEL = 10 mg/kg/day LOAEL = 100 mg/kg/day based on decreased body weight gain in females, increased liver weights in males and slight hepatocellular hypertrophy (centrilobular and midzonal; both sexes)
870.3100	90-Day oral toxicity rodents (mouse)	NOAEL = 100 mg/kg/day LOAEL = 500 mg/kg/day based on increased liver weights, individual cell hepatocellular necrosis and hepatocellular hypertrophy in both sexes
870.3150	90-Day oral toxicity in nonrodents (dog)	NOAEL = 100 mg/kg/day LOAEL = Not identified
870.3200	28-Day dermal toxicity (rat)	NOAEL = 1,000 mg/kg/day LOAEL = Not identified
870.3700	Prenatal developmental in rodents (rat)	Maternal NOAEL = 1,000 mg/kg/day LOAEL = Not identified Developmental NOAEL = 1,000 mg/kg/day LOAEL = Not identified
870.3700	Prenatal developmental in non-rodents (rabbit)	Maternal NOAEL = 80 mg/kg/day LOAEL = 200 mg/kg/day based on inanition, clinical signs, decreased body weights, body weight gains, and food consumption and on increased incidences of abortion Developmental NOAEL = 80 mg/kg/day LOAEL = 200 mg/kg/day based on increased incidences of abortion
870.3800	Reproduction and fertility effects (rat)	Parental/Systemic NOAEL = 100 mg/kg/day LOAEL = Not identified Reproductive NOAEL = 100 mg/kg/day LOAEL = Not identified Offspring NOAEL = 20 mg/kg/day LOAEL = 100 mg/kg/day based on a minimal decrease in $F_{1a}$ pup weights
870.4100	Chronic toxicity rodents	See 870.4300