

TABLE 2.—SUBCHRONIC, CHRONIC, AND OTHER TOXICITY—Continued

Guideline No.	Study Type	Results
870.4200	Carcinogenicity mice	NOAEL = males, 5.7 mg/kg/day; females: 10.9 mg/kg/day LOAEL = males, 234.1 mg/kg/day; females, 475.3 mg/kg/day based on liver toxicity and microscopic lymph node changes in both sexes and increased X-zone vacuolization of the adrenal glands in female mice Evidence of carcinogenicity based on increased incidence of ovarian luteomas
870.5100	Gene Mutation	Negative in a battery of tests
870.5300	Gene Mutation	Negative in a battery of tests
870.5375	Cytogenetics	Negative in battery of tests
870.5395	Cytogenetics	Negative in battery of tests
870.5500	Cytogenetics	Negative in battery of tests
870.5550	Other Effects	Negative
870.6200	Acute neurotoxicity screening battery	NOAEL = males, 11 mg/kg bodyweight (bw); females, 3.1 mg/kg/day LOAEL = males, 22 mg/kg bw; females, 11 mg/kg/day In females, based on reductions in motor and locomotor activity.; in males, (based on FOB observations of slight tremors and ptosis of the eyelids on the day of treatment)
870.6200	Subchronic neurotoxicity screening battery	NOAEL = males, 24.2 mg/kg/day; females, 27.9 mg/kg/day LOAEL = males, 101 mg/kg/day; females, 115 mg/kg/day based on decreased body weight gains and food consumption in both sexes and decreased hindlimb grip strength in males.
870.6300	Developmental neurotoxicity	Maternal NOAEL = 4.4 mg/kg/day LOAEL = 25.6 mg/kg/day based on decreased body weight gain and food consumption during early gestation (gestation day (GD) 0-6. Offspring NOAEL = Tentative Offspring, 4.4 mg/kg/day LOAEL = Tentative Offspring, 25.6 mg/kg/day based on decreased pre-weaning and post-weaning body weights in both sexes and delayed sexual maturation in the males, and altered performance in passive avoidance testing.
870.7485	Metabolism and pharmacokinetics	Thiacloprid is rapidly absorbed and is rapidly excreted after the following metabolic processes, with little remaining in the tissues. The metabolic processes were summarized as: 1. Hydroxylation of the thiazolidine ring and subsequent glucuronidation (as shown by metabolite PIZ 1270), 2. Hydroxylation of the cyanamide moiety (metabolite KNO 1891), 3. Opening of the thiazolidine ring (e.g., metabolites KNO2672, PIZ1297F/WAK 6935), 4. Formation of an oxazole ring (metabolite PIZ 1253), 5. Oxidation and subsequent methylation of the thiazolidine ring (e.g., PIZ 1297E and PIZ 1269X), and 6. Oxidative cleavage of the methylene bridge (PIZ 1243). Only minor gender-related quantitative differences in metabolite profiles were observed.
870.7600	Dermal penetration	A 5% dermal absorption value is appropriate for estimating the risk resulting from dermal exposure to Thiacloprid formulated as a 40.4% liquid formulation (SC 480). This 5% value is also appropriate for other liquid thiacloprid formulations that are similar to the SC 480 liquid formulation product tested and for aqueous dilutions of most thiacloprid formulations.

B. Toxicological Endpoints

The dose at which no adverse effects are observed (the NOAEL) from the toxicology study identified as appropriate for use in risk assessment is used to estimate the toxicological level of concern (LOC). However, the lowest dose at which adverse effects of concern are identified (the LOAEL) is sometimes used for risk assessment if no NOAEL was achieved in the toxicology study selected. An uncertainty factor (UF) is

applied to reflect uncertainties inherent in the extrapolation from laboratory animal data to humans and in the variations in sensitivity among members of the human population as well as other unknowns. An UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intra species differences. As explained in Unit III.D.3., EPA determined that the FQPA SF be reduced to 3X.

For dietary risk assessment (other than cancer) the Agency uses the UF to calculate an acute or chronic reference dose (acute RfD or chronic RfD) where the RfD is equal to the NOAEL divided by the appropriate UF ($RfD = NOAEL / UF$). Where an additional safety factors (SF) is retained due to concerns unique to the FQPA, this additional factor is applied to the RfD by dividing the RfD by such additional factor. The acute or chronic Population Adjusted Dose