

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.

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

(aPAD or cPAD) is a modification of the RfD to accommodate this type of FQPA SF.

For non-dietary risk assessments (other than cancer) the UF is used to determine the LOC. For example, when 100 is the appropriate UF (10X to account for interspecies differences and 10X for intraspecies differences) the LOC is 100. To estimate risk, a ratio of the NOAEL to exposures (margin of exposure (MOE) = $NOAEL / \text{exposure}$) is calculated and compared to the LOC.

A summary of the toxicological endpoints for pyriproxyfen used for human risk assessment is shown in Table 2 of this unit:

TABLE 2.—SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR PYRIPROXYFEN FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and LOC for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13–50 years old and general population	None	None	An appropriate endpoint attributable to a single oral dose was not available in the data base, including maternal toxicity in the developmental toxicity studies.
Chronic Dietary all populations	NOAEL= 35.1 mg/kg/day UF = 100 Chronic RfD = 0.35 mg/kg/day	FQPA SF = 1X $cPAD = cRfD \div FQPA\ SF = 0.35\ mg/kg/day$	Subchronic toxicity and chronic toxicity (feeding)—rat (co-critical) LOAEL = 141.28 mg/kg/day based on decreased body weight and clinical pathology results.
Short-Term Incidental, Oral (1–30 days) Residential	Oral Maternal NOAEL = 100 mg/kg/day	LOC for MOE = 100	Rat developmental toxicity study Maternal LOAEL = 300 mg/kg/day based on decreased body weight, body weight gain, and food consumption, and increased water consumption
Intermediate-Term Incidental, Oral (1–6 months) Residential	Oral NOAEL = 35.1 mg/kg/day	LOC for MOE = 100	Subchronic toxicity and chronic toxicity (feeding)—rat (co-critical) LOAEL = 141.28 mg/kg/day based on decreased body weight and clinical pathology results.
Short-, and Intermediate-Term Dermal (1–30 days and 1–6 months) (Occupational/Residential)	None	None	Based on the systemic toxicity NOAEL of 1,000 mg/kg/day (limit dose) in the 21 day dermal toxicity study in rats, quantification of dermal risks is not required. In addition, no developmental concerns (toxicity) were seen in either rats or rabbits.
Long-Term Dermal (6 months–lifetime) (Occupational/Residential)	Oral NOAEL= 35.1 mg/kg/day (dermal absorption rate = 30%)	LOC for MOE = 100	Subchronic and chronic toxicity (feeding)—rat (co-critical) LOAEL = 141.28 mg/kg/day based decreased body weight and clinical pathology results
Short-, and Intermediate-Term Inhalation (1–30 days and 1–6 months) (Occupational/Residential)	None	None	Based on the absence of significant toxicity at the LOAEL of 1.0 mg/L (limit dose), the quantification of inhalation risks is not required. In addition, no developmental concerns (toxicity) were seen in either rats or rabbits.
Long-Term Inhalation (6 months–lifetime) (Occupational/Residential)	Oral study NOAEL= 35.1 mg/kg/day (inhalation absorption rate = 100%)	LOC for MOE = 100	Subchronic and chronic toxicity (feeding)—rat (co-critical) LOAEL = 141.28 mg/kg/day based on decreased body weight and clinical pathology results