

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/exposure) is calculated and compared to the LOC.

The linear default risk methodology (Q\*) is the primary method currently used by the Agency to quantify carcinogenic risk. The Q\* approach assumes that any amount of exposure will lead to some degree of cancer risk. A Q\* is calculated and used to estimate risk which represents a probability of occurrence of additional cancer cases (e.g., risk is expressed as  $1 \times 10^{-6}$  or one in a million). Under certain specific

circumstances, MOE calculations will be used for the carcinogenic risk assessment. In this non-linear approach, a "point of departure" is identified below which carcinogenic effects are not expected. The point of departure is typically a NOAEL based on an endpoint related to cancer effects though it may be a different value derived from the dose response curve. To estimate risk, a ratio of the point of departure to exposure (MOE<sub>cancer</sub> = point of departure/exposures) is calculated. A summary of the toxicological endpoints for etoxazole used for human risk assessment is shown in Table 2 of this unit:

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

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and LOC for Risk Assessment	Study and Toxicological Effects
Acute dietary (females 13–50 years of age)	NOAEL = None mg/kg/day UF = Not applicable (N/A) Acute RfD = None	FQPA SF = 1X aPAD = acute RfD ÷ FQPA SF = None	A dose and endpoint attributable to a single dose were not identified in the data base including the developmental toxicity studies
Acute dietary (general population including infants and children)	NOAEL = None mg/kg/day UF = N/A Acute RfD = None	FQPA SF = 1X aPAD = acute RfD ÷ FQPA SF = None	A dose and endpoint attributable to a single dose were not identified in the data base including the developmental toxicity studies
Chronic dietary (all populations)	NOAEL = 4.62 mg/kg/day UF = 100 Chronic RfD = 0.046 mg/kg/day	FQPA SF = 1X cPAD = chronic RfD ÷ FQPA SF = 0.046 mg/kg/day	Chronic oral toxicity study - dog LOAEL = 23.5 mg/kg/day based upon increased alkaline phosphatase activity, increased liver weights, liver enlargement (females), and incidences of centrilobular hepatocellular swelling in the liver
Short-term incidental oral (1–30 days)	NOAEL = 4.62 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	Chronic oral toxicity study - dog LOAEL = 23.5 mg/kg/day based upon increased alkaline phosphatase activity, increased liver weights, liver enlargement (females), and incidences of centrilobular hepatocellular swelling in the liver
Intermediate-term incidental oral (1–6 months)	NOAEL = 4.62 mg/kg/day	Residential LOC for MOE = 100 Occupational = NA	Chronic oral toxicity study - dog LOAEL = 23.5 mg/kg/day based upon increased alkaline phosphatase activity, increased liver weights, liver enlargement (females), and incidences of centrilobular hepatocellular swelling in the liver
Short-term dermal (1 to 30 days)	Dermal (or oral) study NOAEL = None	Residential LOC for MOE = N/A Occupational LOC for MOE = N/A	No hazard quantitation required for any duration. No systemic effects noted up to 1,000 mg/kg/day in the 28-day dermal rat study. There are no developmental or reproductive concerns
Intermediate-term dermal (1 to 6 months)	Dermal (or oral) study NOAEL = None	Residential LOC for MOE = N/A Occupational LOC for MOE = N/A	No hazard quantitation required for any duration. No systemic effects noted up to 1,000 mg/kg/day in the 28-day dermal rat study. There are no developmental or reproductive concerns