

408(b)(2) of the FFDCA, for time-limited tolerances for the combined residues of lambda-cyhalothrin and its epimer in or on wild rice at 1.0 ppm, grass forage at 5.0 ppm and grass hay at 6.0 ppm. EPA's assessment of the dietary exposures and risks associated with establishing the tolerances follows.

#### A. 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 endpoint. 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 factor 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 level of concern (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.

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 ( $MOE_{\text{cancer}} = \text{point of departure} / \text{exposures}$ ) is calculated. A summary of the toxicological endpoints for lambda-cyhalothrin used for human risk assessment is shown in the following Table 1:

TABLE 1.— SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR LAMBDA-CYHALOTHRIN FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General population including infants and children)	NOAEL = 0.5 mg/kg/day UF = 100 Acute RfD = 0.005 mg/kg/day	FQPA SF = 1 aPAD = acute RfD/FQPA SF = 0.005 mg/kg/day	Chronic oral study in the dog (lambda-cyhalothrin) LOAEL = 3.5 mg/kg/day based on clinical signs of neurotoxicity (ataxia) observed from day 2, three to seven hours post-dosing.
Chronic Dietary (All populations)	NOAEL = 0.1 mg/kg/day UF = 100 Chronic RfD = 0.001 mg/kg/day	FQPA SF = 1 cPAD = chronic RfD/FQPA SF = 0.001 mg/kg/day	Chronic oral study in the dog (lambda-cyhalothrin) LOAEL = 0.5 based on gait abnormalities observed in 2 dogs
Incidental Oral Short- and Intermediate-Term (1–30 Days and 1–6 Months) Residential Only	NOAEL = 0.1	LOC for MOE = 100 (Residential)	Chronic oral study in the dog (lambda-cyhalothrin) LOAEL = 0.5 based on gait abnormalities observed in 2 dogs
Dermal (All Durations; - Short-Term (1 to 7 days) - Intermediate-Term (1 week to several months) - Long-Term (several months to lifetime) (Residential)	dermal (or oral) study NOAEL = 10 mg/kg/day	LOC for MOE = 100 (Residential)	21-Day dermal toxicity study in the rat (lambda-cyhalothrin) LOAEL = 50 mg/kg/day based on clinical signs of neurotoxicity (observed from day 2) and decreased body weight and body weight gain
Inhalation (All Durations; - Short-Term (1 to 7 days) - Intermediate-Term (1 week to several months) - Long-Term (several months to lifetime) (Residential)	inhalation (or oral) study NOAEL = 0.3 µg/L (0.08 mg/kg/day) (inhalation absorption rate = 100%)	LOC for MOE = 100 (Residential)	21-Day inhalation study in rats (lambda-cyhalothrin) LOAEL = 3.3 µg/L (0.90 mg/kg/day) based on clinical signs of neurotoxicity, decreased body weight gains, increased incidence of punctuate foci in the cornea, slight reductions in cholesterol in females and slight changes in selected urinalysis parameters.
Cancer (oral, dermal, inhalation)			Classification: Group D chemical (not classifiable as to human carcinogenicity)

\*The reference to the FQPA SF refers to any additional SF retained due to concerns unique to the FQPA.