

arising from the missing data and a lack of a NOEL in the DNT study.

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 (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 flufenacet, the Agency concluded that the Special FQPA Safety Factor could be reduced to 1X, based on the low degree of concern and lack of

residual uncertainties for pre- and post-natal toxicity as outlined in Unit III.D.

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 1×10^{-6} or one in a million). Under certain specific circumstances, MOE calculations will be used for the carcinogenicity 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 ($MOE_{cancer} = \text{point of departure/exposures}$) is calculated.

A summary of the toxicological endpoints for flufenacet used for human risk assessment is shown in Table 3 of this unit:

TABLE 3.—SUMMARY OF TOXICOLOGICAL DOSE AND ENDPOINTS FOR FLUFENACET FOR USE IN HUMAN RISK ASSESSMENT

Exposure Scenario	Dose Used in Risk Assessment, UF	Special FQPA SF* and Level of Concern for Risk Assessment	Study and Toxicological Effects
Acute Dietary (General population including infants and children)	LOAEL = 1.7 mg/kg/day UF = 1,000X Acute RfD = LOAEL/UF = 0.0017 mg/kg/day	FQPA SF = 1X aPAD = acute RfD/FQPA SF = 0.0017 mg/kg/day	Developmental Neurotoxicity study in rats. LOAEL = 1.7 mg/kg/day based on decreased body weight/body weight gain, and missing morphometric measurements in caudate/putamen, in pups.
Chronic Dietary (All populations)	LOAEL = 1.7 mg/kg/day UF = 1,000 Chronic RfD = LOAEL/UF = 0.0017 mg/kg/day	FQPA SF = 1X cPAD = chronic RfD/ FQPA SF = 0.0017 mg/kg/day	Developmental Neurotoxicity study in rats. LOAEL = 1.7 mg/kg/day based on decreased body weight/body weight gain in pups.
Cancer (oral, dermal, inhalation)	Classified as 'Not Likely' to be a carcinogen.		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no-observed-adverse-effect-level, LOAEL = lowest-observed-adverse-effect-level, PAD = population-adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable/Not Required.

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

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Tolerances have been established (40 CFR 180.527) for the combined residues of flufenacet, *N*-(4-fluorophenyl)-*N*-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]acetamide and its metabolites containing the 4-fluoro-*N*-methylethyl benzenamine moiety, in or on a variety of raw agricultural commodities. Tolerances have been established on meat, fat, kidney, and meat byproducts of cattle, goats, hogs, horses, and sheep, wheat grain, forage, hay, and straw in connection with a section 18. These tolerances expire July, 2005 and have been included in the risk assessments. Risk assessments were conducted by EPA to assess dietary exposures from flufenacet in food as follows:

i. *Acute exposure.* Acute dietary risk assessments are performed for a food-

use pesticide if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a one day or single exposure. The Dietary Exposure Evaluation Model (DEEM) analysis evaluated the individual food consumption as reported by respondents in the USDA [1994–1996 and 1998] nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The following assumptions were made for the acute exposure assessments:

a. Anticipated-residue estimates were assumed for some commodities (field corn, soybeans, and wheat);

b. Tolerance-level residues were assumed for some crops (cereal grains); and

c. Percent crop-treated estimates were utilized for all crops.

ii. *Chronic exposure.* In conducting this chronic dietary risk assessment the

Dietary Exposure Evaluation Model (DEEM) analysis evaluated the individual food consumption as reported by respondents in the USDA [1994–1996 and 1998] nationwide Continuing Surveys of Food Intake by Individuals (CSFII) and accumulated exposure to the chemical for each commodity. The following assumptions were made for the chronic exposure assessments:

a. Anticipated-residue estimates were assumed for some commodities (field corn, soybeans, and wheat);

b. Tolerance-level residues were assumed for some crops (cereal grains); and

c. Percent crop-treated estimates were utilized for all crops.

iii. *Cancer.* Flufenacet is not carcinogenic, therefore a quantitative cancer risk assessment was not performed.