

65 ppm; longan, lychee, pulasan, rambutan, and spanish lime at 1.0 ppm; and turnip, greens at 10 ppm. EPA's assessment of exposures and risks associated with establishing the tolerances follow.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children. The nature of the toxic effects caused by fludioxonil are discussed in Unit III.A. of the final rule on fludioxonil, which published in the **Federal Register** of December 29, 2000 (65 FR 82927) (FRL-6760-9), and August 2, 2002 (67 FR 50354) (FRL-7188-7).

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.

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 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 fludioxonil used for human risk assessment is Unit III.B. of the final rule on fludioxonil, which published in the **Federal Register** of December 29, 2000 (65 FR 82927) and August 2, 2002 (67 FR 50354).

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Tolerances have been established (40 CFR 180.516) for the residues of fludioxonil, in or on a variety of raw agricultural commodities. Fludioxonil is registered for foliar application (grape, strawberry, green onion, dry bulb onion, bushberry, caneberry, juneberry, longonberry, pistachio, salal, and watercress), post-harvest application (stone fruit), and for seed treatment purposes (numerous crops) with tolerances for residues of fludioxonil ranging from 0.01-7.0 ppm (40 CFR 180.516(a)). A section 18 registration is also established for post-harvest application to pomegranate with a tolerance for residues of fludioxonil of 5.0 ppm (40 CFR 180.516(b)). Currently there are no tolerances established for residues of fludioxonil in/on livestock. Risk assessments were conducted by EPA to assess dietary exposures from fludioxonil 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 1-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, 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: The acute analysis assumed tolerance level residues, 100% crop treatment (CT), and DEEM (ver. 7.76) default processing factors for all registered/proposed commodities (tier 1).

ii. *Chronic exposure.* In conducting this chronic dietary risk assessment the DEEM analysis evaluated the individual food consumption as reported by respondents in the USDA 1994-1996, 1998 nationwide CSFII and accumulated exposure to the chemical for each commodity. The following assumptions were made for the chronic exposure assessments: The chronic analysis assumed tolerance level residues, 100% CT, and DEEM (ver. 7.76) default processing factors for all registered/proposed commodities (tier 1).

iii. *Cancer.* EPA's Cancer Peer Review Committee (CPRC) classified fludioxonil as a Group D - not classifiable as to human carcinogenicity.

2. *Dietary exposure from drinking water.* The Agency lacks sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for fludioxonil in drinking water. Because the Agency does not have comprehensive monitoring data, drinking water concentration estimates are made by reliance on simulation or modeling taking into account data on the physical characteristics of fludioxonil.

The Agency uses the First Index Reservoir Screening Tool (FIRST) or the Pesticide Root Zone model/Exposure Analysis Modeling System (PRZM/EXAMS), to produce estimates of pesticide concentrations in an index reservoir. The Screening Concentration in Ground Water (SCI-GROW) model is used to predict pesticide concentrations in shallow ground water. For a screening-level assessment for surface water EPA will use FIRST (a tier 1 model) before using PRZM/EXAMS (a tier 2 model). The FIRST model is a subset of the PRZM/EXAMS model that uses a specific high-end runoff scenario for pesticides. FIRST and PRZM/EXAMS incorporate an index reservoir environment, and a percent crop area factor as an adjustment to account for the maximum percent crop coverage within a watershed or drainage basin.

None of these models include consideration of the impact processing (mixing, dilution, or treatment) of raw