

infants and children. The nature of the toxic effects caused by azoxystrobin are discussed in Unit III.A of the Final Rule on Azoxystrobin Pesticide Tolerance published in the **Federal Register** on September 20, 2002 (67 FR 59169)(FRL-7198-9).

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. A UF of 100 is routinely used, 10X to account for interspecies differences and 10X for intraspecies 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 (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 azoxystrobin used for human risk assessment is discussed in Unit III.B. of the Final Rule on Azoxystrobin Pesticide Tolerance published in the **Federal Register** on September 20, 2002 (67 FR 59169)(FRL-7198-9).

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Tolerances have been established (40 CFR 180.507) for the combined residues of azoxystrobin, in or on a variety of raw agricultural commodities. Tolerances have been established for residues of azoxystrobin in or on a variety of raw agricultural commodities at levels ranging from 0.01 ppm (pecans) to 55 ppm (soybean hay), and on meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep at levels ranging from 0.01 to 0.07 ppm, and on milk at 0.006 ppm. A time-limited tolerance (to expire on 12/31/2003) is currently established at 30 ppm for the head and stem Brassica vegetables, subgroup 5A. Risk assessments were conducted by EPA to assess dietary exposures from azoxystrobin 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. In conducting this acute risk assessment, EPA used the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™) which incorporates food consumption data 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 assumption was made for the acute exposure assessment: A Tier 1 acute dietary exposure analysis was performed for azoxystrobin.

ii. *Chronic exposure.* In conducting this chronic risk assessment, EPA used the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™) which incorporates food consumption data 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: The chronic dietary exposure analysis was performed for the general U.S. Population and all population subgroups using tolerance level residues (livestock) and total residues of concern (plants; parent and metabolites) and 100% crop treated data for the proposed commodities and all registered uses.

iii. *Cancer.* EPA's Cancer Assessment Review Committee (CARC) evaluated the carcinogenic potential of azoxystrobin and classified azoxystrobin as "not likely to be a human carcinogen" based on the revised Cancer Guidelines.

2. *Dietary exposure from drinking water.* The Agency lacks sufficient monitoring exposure data to complete a comprehensive dietary exposure analysis and risk assessment for azoxystrobin 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 azoxystrobin.

The Agency uses the FQPA 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 groundwater (SCI-GROW) model is used to predict pesticide concentrations in shallow groundwater. 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 water for distribution as drinking water would likely have on the removal of pesticides from the source water. The primary use of these models by the Agency at this stage is to provide a coarse screen for sorting out pesticides for which it is highly unlikely that drinking water concentrations would ever exceed human health levels of concern.