

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. For further discussion of the regulatory requirements of section 408 of the FFDCA and a complete description of the risk assessment process, see the final rule on Bifenthrin Pesticide Tolerances (62 FR 62961, November 26, 1997) (FRL-5754-7).

III. Aggregate Risk Assessment and Determination of Safety

Consistent with section 408(b)(2)(D) of the FFDCA, EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure, consistent with section 408(b)(2) of the FFDCA, for a tolerance for residues of fosetyl-Al on onion, green at 10 ppm. EPA's assessment of exposures and risks associated with establishing the tolerance follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data on fosetyl-Al and considered their 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 fosetyl-Al are discussed in the **Federal Register** of August 18, 2000 (65 FR 50431) (FRL-6599-4) as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies reviewed. Please refer to this document should you desire detailed toxicological information on fosetyl-Al.

B. Toxicological Endpoints

The dose at which 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 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 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 fosetyl-Al used for human risk assessment is discussed in Unit III. B. of the final rule on fosetyl-Al tolerances published in the **Federal Register** on August 29, 2002 (67 FR 55339) (FRL-7195-1).

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* Tolerances have been established (40 CFR 180.415) for the residues of fosetyl-Al, in or on a variety of raw agricultural commodities. Residues of fosetyl-Al are currently regulated under 40 CFR 180.415(a) in bushberry subgroup, and juneberry, lingonberry, and salal, at 40 ppm; caneberries, fresh ginseng root, pineapple, pineapple fodder and forage

at 0.1 ppm; onions (dry bulb) at 0.5 ppm, macadamia nuts at 0.2 ppm; cranberry at 0.5 ppm; fruit, citrus, group at 5.0 ppm; pea, succulent at 0.3 ppm; tomatoes and bananas at 3.0 ppm; pome fruit at 10 ppm; cucurbit vegetables group at 15 ppm; avocados at 25 ppm; hops, dried at 45 ppm; brassica (cole) leafy vegetables group at 60 ppm; strawberries at 75 ppm; turnip, roots at 15 ppm; turnip, tops at 40 ppm; and leafy vegetables (except brassica vegetables) group at 100 ppm. Time-limited tolerances associated with a section 18 request for the residues of fosetyl-Al have been granted in/on peas, succulent at 1.0 ppm under 40 CFR 180.415(b) which expired September 31, 2000. Additionally, tolerances are established in 40 CFR 180.415(c) for residues of fosetyl-Al in/on asparagus at 0.1 ppm and grapes at 10 ppm in conjunction with regional registrations. Risk assessments were conducted by EPA to assess dietary exposures from fosetyl-Al 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. No appropriate endpoint attributable to a single exposure (dose) of fosetyl-Al was identified from the oral toxicity studies including developmental toxicity studies in rats and rabbits. Therefore, fosetyl-Al is not expected to pose an acute risk.

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 1989-1992 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 Tier 1 (assuming tolerance level residues and 100% crops treated for all commodities) chronic dietary exposure assessment was conducted for all supported fosetyl-Al food uses. Chronic dietary exposure estimates were provided for the general U.S. population and various population subgroups.

iii. *Cancer.* The Agency concludes that pesticidal use of fosetyl-Al is unlikely to pose a carcinogenic hazard to humans. Therefore, a cancer dietary exposure analysis for fosetyl-Al was not performed.

2. *Dietary exposure from drinking water.* Fosetyl-Al is not expected to reach ground water or surface water under most conditions.