

228.9 mg/kg/day for male rats and 281.5 mg/kg/day for females), based on increased incidences of retinal atrophy. The chronic NOAEL is 1,000 ppm. Under the conditions of this study, there was no evidence of carcinogenic potential. Dosing was considered adequate based on the increased incidence of retinal atrophy.

6. *Animal metabolism.* Studies conducted in rats using ^{14}C -glufosinate-ammonium have shown that the compound is poorly absorbed (5-10%) after oral administration and is rapidly eliminated primarily as the parent compound. The highest residue levels were found in liver and kidney tissues.

The metabolic profile and the quantitative distribution of metabolites were very similar in both goat and hen. The vast majority of the dose was excreted, primarily as parent compound. The very limited residues found in edible tissues, milk and eggs were comprised principally of glufosinate and 3-methylphosphinico-propionic acid (Hoe 061517), with lesser amounts of *N*-acetyl-*L*-glufosinate (Hoe 099730) and 2-methylphosphinico-acetic acid (Hoe 064619).

7. *Metabolite toxicology.* Additional testing has been conducted with the major metabolites, 3-methylphosphinico-propionic acid, and *N*-acetyl-*L*-glufosinate. Based on subchronic and developmental toxicity study results, a profile of similar or less toxicity was observed for the metabolites as compared to the parent compound, glufosinate-ammonium.

8. *Endocrine disruption.* No special studies have been conducted to investigate the potential of glufosinate-ammonium to induce estrogenic or other endocrine effects. However, no evidence of estrogenic or other endocrine effects have been noted in any of the toxicology studies that have been conducted with this product and there is no reason to suspect that any such effects would be likely.

C. Aggregate Exposure

1. *Dietary exposure.* Tolerances have been established (40 CFR 180.473) for the combined residues of glufosinate-ammonium and metabolites in or on a variety of raw agricultural commodities. No appropriate toxicological endpoint attributable to a single exposure was identified in the available toxicity studies. EPA has, therefore, not established an acute reference dose (RfD) for the general population including infants and children. An acute population adjusted dose (aPAD - 95th percentile) of 0.021 mg/kg/day was established, however, for the females 13+ subgroup based on the results of the

developmental toxicity study in rabbits with an uncertainty factor of 300. Therefore, an acute dietary analysis was conducted for this sub-population; whereas, chronic dietary analysis was conducted for the usual populations. A chronic population adjusted dose (cPAD) of 0.007 mg/kg/day (based on the 2-year chronic study in rats and an uncertainty factor of 300) was used to perform the chronic dietary analysis.

i. *Food.* An acute dietary analysis was conducted using the Dietary Exposure Evaluation Model (DEEMTM) software version 7.6 and the 1994–1998 Continuing Survey of Food Intake by Individuals (CSFII) consumption data base. The Tier I acute dietary assessment was modified by incorporating percent crop treated (PCT) values for blended items only. Thus, the following PCT values were used: Soybean, 6%; canola, 11%; cotton, 15%, rice, 2%; sugar beet, 1%; and sugar beet molasses, 1%. Tolerance values of blended feed items in the animal diets were also multiplied by PCT. Dietary burdens were then multiplied by the maximum tissue to feed ratios observed in the animal feeding studies. This Tier I analysis resulted in an exposure of 0.002746 mg/kg bw/day (95th percentile) for the female 13+ sub-population (the only population of concern) representing 13% utilization of the aPAD.

Chronic dietary analysis was conducted to estimate exposure to potential glufosinate-ammonium residues in or on registered and proposed commodities. The DEEMTM software (version 7.6) and the 1994–1998 USDA food consumption data were used. Tolerance level residues were assumed for all commodities. Percent crop treated values generated by EPA/BEAD and Bayer CropScience were incorporated as follows: Tree nuts, 1%; apples, 1%; field corn, 3%; grapes, 1%; soybeans, 6%; potatoes, 1%; canola, 11%; and sugar beet, 1%. Bayer CropScience estimates that an upper bound value for cotton at market maturity is 15% and that for rice is 2%. All other crops are included at 100% of crop treated. For the chronic dietary risk assessment, secondary residues that could occur as a result of residues of glufosinate-ammonium and metabolites in the diet of ruminants and poultry were adjusted for percent of the crop treated as indicated above. Chronic dietary exposure estimates from residues of glufosinate-ammonium for the U.S. population represented approximately 3.2% of the chronic PAD; whereas that for children 1-2, the sub-population with the highest exposure, represented approximately 12% of the

chronic PAD. The approach used is very conservative, yet still indicates that dietary exposures for all segments of the population are well within the chronic reference doses. This analysis was based on highly conservative assumptions. The Agency has no concerns with PAD utilization up to 100%.

ii. *Drinking water.* U.S. EPA's Standard Operating Procedure (SOP) for Drinking Water Exposure and Risk Assessments was used to perform the drinking water assessment. The models Screening Concentrations in Ground Water (SCI-GROW) and EPA's Pesticide Root Zone Model/Exposure Analysis Modeling System (PRZM/EXAMS) were used to estimate the concentration of glufosinate-ammonium that might occur in water. The acute drinking water level of comparison (DWLOC) for females 13+ is 548 parts per billion (ppb). In comparison, the acute estimated drinking water concentrations (EDWC) calculated by PRZM/EXAMS is 67 ppb.

The chronic DWLOC calculated for adults is 237 ppb and that for children/toddlers is 62 ppb. The chronic EDWC calculated using a worst case scenario is 17 ppb PRZM/EXAMS. The DWLOCs are based on highly conservative dietary (food) exposures and are expected to be much higher in real world situations reducing further the percent utilization of the DWLOC.

2. *Non-dietary exposure.* U.S. EPA's SOP for Drinking Water Exposure and Risk Assessments was used to perform the drinking water assessment. The models SCI-GROW and PRZM/EXAMS were used to estimate the concentration of glufosinate-ammonium that might occur in water. The acute DWLOC for females 13+ is 548 ppb. In comparison, the acute EDWC calculated by PRZM/EXAMS is 67 ppb.

The chronic DWLOC calculated for adults is 237 ppb and that for children/toddlers is 62 ppb. The chronic EDWC calculated using a worst case scenario is 17 ppb PRZM/EXAMS. The DWLOCs are based on highly conservative dietary (food) exposures and are expected to be much higher in real world situations reducing further the percent utilization of the DWLOC.

D. Cumulative Effects

Section 408(b)(2)(D)(v) requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." EPA has indicated that, at this time, the Agency does not have available data to determine whether glufosinate-