

EPA does not have, at this time, available data to determine whether glufosinate ammonium has a common mechanism of toxicity with other substances. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, EPA has not made a common mechanism of toxicity finding for glufosinate ammonium and any other substances and glufosinate ammonium does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action; therefore, EPA has not assumed that glufosinate ammonium has a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the cumulative effects of such chemicals, see the policy statements released by EPA's Office of Pesticide Programs concerning common mechanism determinations and procedures for cumulating effects from substances found to have a common mechanism on EPA's website at <http://www.epa.gov/pesticides/cumulative/>.

D. Safety Factor for Infants and Children

1. *In general.* Section 408 of the FFDCA provides that EPA shall apply an additional tenfold margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the data base on toxicity and exposure unless EPA determines that a different margin of safety will be safe for infants and children. Margins of safety are incorporated into EPA risk assessments either directly through use of a MOE analysis or through using uncertainty (safety) factors in calculating a dose level that poses no appreciable risk to humans.

2. *Prenatal and postnatal sensitivity.* The studies examining prenatal and postnatal toxicity showed:

a. No quantitative or qualitative evidence of increased susceptibility following *in utero* exposure in the prenatal developmental study in rats.

b. Qualitative evidence of increased susceptibility in the prenatal developmental study in rabbits and quantitative evidence of increased susceptibility in the 2-generation reproduction study in rats. In this study, a decrease in the number of viable pups was observed in the absence of parental toxicity at any dose.

Since there is qualitative evidence of increased susceptibility of the young following exposure to glufosinate

ammonium, EPA performed a degree of concern analysis to: Determine the level of concern for the effects observed when considered in the context of all available toxicity data; and identify any residual uncertainties after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment of this chemical. In the rabbit developmental study the degree of concern observed as low noting that the fetal effects of concern occurred only at the highest dose tested and that a clear NOAEL for effects was established. In the 2-generation reproduction study the degree of concern for the effects observed as low noting that clear NOAELs and LOAELs were identified for the offspring effects of concern and the dose-response well-characterized.

3. *Conclusion.* There is not an adequate toxicity data base for glufosinate ammonium and its metabolites although the exposure data are complete or are estimated based on data that reasonably account for potential exposures. EPA identified the following data gaps:

a. Acute neurotoxicity study conducted in the rat which includes glutamine synthetase activity measurement in the liver, kidneys, and brain.

b. A developmental neurotoxicity (DNT) study conducted in the rat which includes comparative glutamine synthetase activity measurement in the liver, kidneys, and brain of the pups and mothers.

c. A 28-day inhalation toxicity study in rats with glutamine synthetase activity measurements in brain, kidney, liver and lung.

EPA is also requesting additional data to confirm that liver and kidney changes, observed in the absence of histopathological changes, are an adaptive response and not an adverse effect. These studies are required because the glutamine synthetase measurements are not available in young and adult animals. Therefore, EPA has applied additional data base uncertainty factors in this risk assessment. The results of these studies are expected to eliminate any uncertainty that may be associated in characterizing the toxicity of glufosinate ammonium.

For dietary risk assessment, an FQPA additional 10X safety factor, retained as a data base uncertainty factor due to the lack of a developmental neurotoxicity (DNT) study that measures glutamine synthetase activity in the young and adult animals, was applied to all dietary and residential dermal, inhalation, and incidental oral exposure assessments. For residential inhalation exposure

assessments an additional 10x data base uncertainty factor was applied due to the lack of an adequate inhalation study and high concern for exposure via the inhalation route with a total uncertainty factor of 3,000 applied based on EPA policy cited in Unit III.B.

E. Aggregate Risks and Determination of Safety

To estimate total aggregate exposure to a pesticide from food, drinking water, and residential uses, the Agency calculates DWLOCs which are used as a point of comparison against the model estimates of a pesticide's concentration in water (EECs). DWLOC values are not regulatory standards for drinking water. DWLOCs are theoretical upper limits on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food and residential uses. In calculating a DWLOC, the Agency determines how much of the acceptable exposure (i.e., the PAD) is available for exposure through drinking water [e.g., allowable chronic water exposure (mg/kg/day) = cPAD - (average food + residential exposure)]. This allowable exposure through drinking water is used to calculate a DWLOC.

A DWLOC will vary depending on the toxic endpoint, drinking water consumption, and body weights. Default body weights and consumption values as used by the USEPA Office of Water are used to calculate DWLOCs: 2 liter (L)/70 kg (adult male), 2L/60 kg (adult female), and 1L/10 kg (child). Default body weights and drinking water consumption values vary on an individual basis. This variation will be taken into account in more refined screening-level and quantitative drinking water exposure assessments. Different populations will have different DWLOCs. Generally, a DWLOC is calculated for each type of risk assessment used: Acute, short-term, intermediate-term, chronic, and cancer.

When EECs for surface water and groundwater are less than the calculated DWLOCs, EPA concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which EPA has reliable data) would not result in unacceptable levels of aggregate human health risk at this time. Because EPA considers the aggregate risk resulting from multiple exposure pathways associated with a pesticide's uses, levels of comparison in drinking water may vary as those uses change. If new uses are added in the future, EPA will reassess the potential impacts of residues of the pesticide in drinking water as a part of the aggregate risk assessment process.