

to water-soluble products that may be formed due to microbial and/or photodegradative action.

2. *Magnitude of residue at the time of harvest and method used to determine the residue.* Crops in residue trials were treated at maximum label rates and harvested at the specified minimum treatment to harvest intervals. Residue data previously submitted by Abbott Laboratories and reviewed by EPA indicated that at the proposed use rates, no quantifiable residues were present in or on the food commodities at 21 days after treatment. Additional residue data generated internationally has been provided to EPA by Valent BioSciences Corporation. There is a practical method for detecting and measuring levels of aviglycine HCl in or on food with a limit of detection (LOD) that allows monitoring of food with residues at or above the levels set in these proposed tolerances. Abbott Laboratories has submitted a practical analytical methodology for detecting and measuring levels of aviglycine HCl in or on raw agricultural commodities (RACs). The proposed analytical method for determining residues is by high-performance liquid chromatography (HPLC). The HPLC/fluorescence detector analytical method used in the residue studies has been validated by an independent laboratory and provided to FDA. The limit of quantitation (LOQ) was 0.075 µg/kg.

3. *A statement of why an analytical method for detecting and measuring the levels of the pesticide residue are not needed.* *Analytical Enforcement Methodology.* Adequate enforcement methodology high performance liquid chromatography (HPLC)/fluorescence detector) is available to enforce the tolerance expression. The method may be requested from: Christine Olinger, Acting Chief of the Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Fort Meade, MD 20755-5350; telephone number: (410) 305-2905; e-mail address: [residuemethods@epa.gov](mailto:residuemethods@epa.gov).

#### C. Mammalian Toxicological Profile

1. *Acute toxicity.* Aviglycine HCl has low acute oral, dermal, and inhalation toxicity. The oral lethal dose (LD)<sub>50</sub> in rats is >5,000 milligrams/kilogram (mg/kg), the dermal LD<sub>50</sub> is >2,000 mg/kg and the inhalation 4-hour lethal concentration (LC)<sub>50</sub> is >5.00 milligrams/Liter (mg/L) air. Aviglycine HCl is not a skin sensitizer in guinea pigs, and is not irritating to the skin and eyes of rabbits. End-use formulations of aviglycine HCl have similar low acute toxicity profiles.

2. *Genotoxicity.* Aviglycine HCl does not induce gene mutations in bacterial and mammalian cells, chromosome aberrations in mammalian cells or deoxyribonucleic acid (DNA) damage in bacterial cells in *in vitro* test systems. Similarly, it does not exhibit a clastogenic effect *in vivo* in the rat micronucleus test. Therefore, there is no evidence to suggest a genotoxic hazard at any of the three main levels of genetic organization.

3. *Reproductive and developmental toxicity.* In the rabbit developmental toxicity study with aviglycine HCl, there was no evidence of teratogenicity or other embryotoxic effects at the highest dose levels tested, although maternal toxicity was evident. The rabbit maternal no observed adverse effect level (NOAEL) was established at 0.4 mg a.i./kg body weight/day (mg a.i./kg bwt/day) based on reduced body weight gains and food consumption, and decreased defecation. The developmental NOAEL was established at 0.4 mg a.i./kg bwt/day based on fetal body weights. In the rat test the maternal NOAEL was established at 1.77 mg a.i./kg bwt/day based on inhibition of body weight gain and reduced food consumption. The developmental NOAEL was found to be 1.77 mg a.i./kg bwt/day based on decreased mean fetal body weights and reduced ossification at a higher dose level. The developmental and maternal lowest observed adverse effect levels (LOAELs) were established at 8.06 mg a.i./kg bwt/day. Aviglycine HCl was evaluated in a rat 2-generation reproduction study submitted by Abbott Laboratories. Based on reductions in body weight, changes in organ weights and an increased incidence of microscopic findings at the 2.5 mg a.i./kg bwt/day dose, the parental NOAEL was established at 0.8 mg a.i./kg bwt/day. The NOAEL for reproductive toxicity was established at 4.0 mg a.i./kg bwt/day and the neonatal toxicity NOAEL was established at 2.5 mg a.i./kg bwt/day.

4. *Subchronic toxicity.* Subchronic 90-day feeding studies were conducted with rats, mice, and dogs. In a 90-day feeding study in rats, the NOAEL was 0.4 mg a.i./kg bwt/day for males and females based on increased incidence of periportal hepatocellular vacuolation in the liver. In the 90-day feeding study in mice, the NOAEL was established at 10 mg a.i./kg bwt/day for males and females - based on decreased body weight and histopathological changes in the liver (both sexes), in the testis (males) and the adrenal (females) at 25 mg a.i./kg bwt/day. For dogs, the NOAEL was established at 0.6 mg a.i./

kg bwt/day - based on inappetence, low body weight gain and centrilobular histopathological changes in the liver at 1.2 mg a.i./kg bwt/day. Note that the liver vacuolation is considered an adaptive change. Increased vacuolation of the liver was not observed in the 52-week chronic rat study or the 104-week rat oncogenicity study. A 21-day repeat dose dermal toxicity study in rats was carried out at 0, 100, 500, and 1,000 mg a.i./kg bwt/day. The NOAEL is 1,000 mg a.i./kg bwt/day; a LOAEL was not determined.

5. *Chronic toxicity.* Chronic studies with aviglycine HCl were conducted on rats to determine oncogenic potential and/or chronic toxicity of the compound. The NOAEL for the 1-year chronic study was 0.7 mg a.i./kg bwt/day for males and females based on decreases in body weights, food consumption, testicular tubular, epithelial vacuolation, and pancreatic acinar cell atrophy. The rat carcinogenicity study with aviglycine HCl confirmed the substance has no carcinogenic potential. There was no evidence of cell necrosis that could be a preliminary stage to active ingredient tumor genesis, and time of death was similar to controls. During the 2-year carcinogenicity study, the administration of aviglycine HCl at 7 mg a.i./kg bwt/day was associated with body weight and food consumption reductions, increases in the incidence of adrenal focal medullary cell hyperplasia, testicular tubular atrophy, and other associated findings in the testis and epididymis, ocular cataracts, and pancreatic lobular/acinar cell atrophy. The NOAEL was established at 0.7 mg a.i./kg bwt/day.

#### D. Aggregate Exposure

1. *Dietary exposure—i. Food.* Expected dietary exposures from residues of aviglycine HCl would occur through apples, pears, and processed apples and pears. Chronic dietary exposure assessments were conducted using a Tier I approach. This Tier I assessment incorporated tolerance level residues and 100% crop-treated in the estimated dietary intake trends. The resulting exposures were compared to a RfD of 0.007 mg a.i./kg bwt/day, which was based on the NOAEL of 0.7 mg a.i./kg bwt/day from the 104-week rat study and a 100-fold uncertainty factor (UF). Chronic dietary exposure estimates for the overall U.S. population and 25 population subgroups are well below the chronic RfD. There are no acute toxicity concerns with aviglycine HCl as there is no toxicological endpoint attributable to a single exposure in the aviglycine HCl toxicology data base,