

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.* There is no evidence (qualitative or quantitative) for increased susceptibility following *in utero* exposure in the developmental toxicity studies in rats and rabbits or prenatal/postnatal exposure in the 2-generation reproduction study in rats. In both the rat and rabbit developmental toxicity studies maternal toxicity included decreased body weight gain. No developmental toxicity was noted in rats up to the highest dose tested of 225 mg/kg/day. Developmental toxicity in rabbits (increased post implantation loss) occurred at a higher dose than maternal toxicity. In the 2-generation reproduction study in rats, parental and offspring toxicity included body weight decrements at similar doses. No reproductive effects were noted up to the highest dose tested.

3. *Conclusion.* EPA evaluated the potential for increased susceptibility of infants and children from exposure to chlorfenapyr. EPA concluded that the toxicology data base was incomplete for FQPA purposes because a required DNT has not been submitted. The DNT was required due to the presence of neuropathology (central nervous system lesions) and neurotoxic signs seen in adult rats (males) and mice (both sexes). Other than lacking the DNT study, EPA identified no residual uncertainties for prenatal/postnatal toxicity. This decision is based on the following:

- There is no evidence (qualitative or quantitative) of increased susceptibility of rat or rabbit fetuses to *in utero* exposure in developmental toxicity studies. There is no evidence (qualitative or quantitative) of increased susceptibility of rat offspring in the multi-generation reproduction toxicity study.
- There are no concerns or residual uncertainties for prenatal and postnatal toxicity in the available developmental and 2-generation reproduction toxicity studies.
- The conservative residue assumptions used in the dietary exposure risk assessments, and the completeness of the residue chemistry database.

EPA concluded that a FQPA SF in the form of UFDB of 10X is required until the data from the DNT study are received and evaluated. EPA does not have sufficient reliable data justifying the selection of a factor lower than the default 10X value for this data gap.

#### E. Aggregate Risks and Determination of Safety

1. *Acute risk.* Using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure from food to chlorfenapyr will occupy 6% of the aPAD for the U.S. population, 15% of the aPAD for females 13 years and older, 12% of the aPAD for children 1–2 years old and 3% of the aPAD for infants < 1 year old. As explained in Unit III.C.2., there is no potential for acute dietary exposure to chlorfenapyr in drinking water. EPA does not expect the aggregate exposure to exceed 100% of the aPAD.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to chlorfenapyr from food will utilize 24% of the cPAD for the U.S. population, 10% of the cPAD for infants < 1 year old and 47% of the cPAD for children 1–2 years old. Based on the use pattern, chronic residential exposure to residues of chlorfenapyr is not expected. There is no potential for chronic dietary exposure to chlorfenapyr in drinking water. EPA does not expect the aggregate exposure to exceed 100% of the cPAD.

3. *Short-term risk.* Short-term aggregate exposure takes into account residential exposure plus chronic exposure to food and water (considered to be a background exposure level). Chlorfenapyr is registered for use on sites that would result in negligible residential exposure and no exposure from drinking water. Therefore, the aggregate risk is equal to the risk from

food, and does not exceed the Agency's LOC.

#### IV. Other Considerations

##### A. Analytical Enforcement Methodology

1. *Residue analytical methods.* The proposed enforcement method is M2427, a gas chromatography/electron capture detection (GC/ECD) method with an limit of quantitation (LOQ) of 0.05 ppm. Method M2427 has been subjected to a successful independent laboratory validation (ILV) as well as an acceptable radiovalidation using samples obtained from lettuce and tomato metabolism studies. A version of this method, M2284 was sent to EPA's Analytical Chemistry Branch (ACB) in Beltsville, MD for a petition method validation (PMV) on oranges and citrus oil. Although the PMV was successful, minor revisions were required. A new version of analytical method M2284 with the recommended revisions has not been submitted. The Agency's review of PP 6F4716 concluded that method M2427 is adequate for data collection and tolerance enforcement purposes pending submission of the rewritten method M2284. Since M2427 is similar to M2284, the petitioner was directed to rewrite Method M2427 following the ACB comments regarding M2284. The petitioner has submitted Method 2427.02, which contains the requested revisions.

2. *Multiresidue method (MRM).* The data requirement for MRM is satisfied pending U.S. Food and Drug Administration (FDA) review and acceptance of the MRM results. The petitioner previously submitted MRM recovery data for chlorfenapyr through FDA Protocols A through E. Protocols A and B were not applicable to chlorfenapyr. In Protocol C, chlorfenapyr gave a good response with the electron capture detector on three different GC columns. In Protocol D, using pears as a non-fatty food representative, the 5% OV-101 column gave the greatest sensitivity at 0.05 and 0.50 ppm. In Protocol E, chlorfenapyr eluted well on Florisil in both the ethyl ether/petroleum ether system and the alternate hexane/acetonitrile/methylene chloride system and gave acceptable recovery.

Adequate enforcement methodology is available to enforce the tolerance expression. The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755–5350; telephone number: (410) 305–2905; e-mail address: [residuemethods@epa.gov](mailto:residuemethods@epa.gov).