

a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, and from residential uses. Since DWLOCs address total aggregate exposure to flumioxazin they are further discussed in the aggregate risk sections below.

The hydrolysis study for flumioxazin indicates that flumioxazin forms the metabolite 482-HA, which can further hydrolyze to metabolites APF and THPA. The rates of the two hydrolytic reactions are very pH dependent, but the parent is not very stable at any likely environmental pH. Additional data indicated that THPA and APF are likely to be very mobile. Although THPA can comprise a major portion of the total residue in water, it does not possess the phenyl ring and is thus considered significantly less toxic than parent, APF, and 482-HA, thus THPA needs not be included in the residue of concern for drinking water. Therefore, parent flumioxazin and the metabolites 482-HA and APF are the residues of concern in drinking water.

Based on the GENEEC and SCI-GROW models the EECs of flumioxazin for acute exposures are estimated to be 2.4 parts per billion (ppb) for surface water and 6.3 ppb for ground water. The EECs for chronic exposures are estimated to be 0.67 ppb for surface water and 6.3 ppb for ground water.

3. *From non-dietary exposure.* The term "residential exposure" is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). Flumioxazin is not registered for use on any sites that would result in residential exposure.

4. *Cumulative exposure to substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of the FFDCA 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 does not have, at this time, available data to determine whether flumioxazin has a common mechanism of toxicity with other substances or how to include this pesticide in a cumulative risk assessment. Unlike other pesticides for which EPA has followed a cumulative risk approach based on a common mechanism of toxicity, flumioxazin 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 flumioxazin 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 final rule for Bifenthrin Pesticide Tolerances (62 FR 62961, November 26, 1997).

### C. 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 data for flumioxazin indicate that there is both quantitative and qualitative evidence of increased susceptibility to flumioxazin from prenatal or postnatal exposures. Quantitative susceptibility is observed when the young respond more than the adults at a given dose, and qualitative susceptibility is observed when there is a unique biological target, such as the developing brain, that predisposes the individual. The quantitative and qualitative evidence of increased susceptibility is observed with the rat fetuses to *in utero* exposure to flumioxazin in the oral and dermal developmental studies. In both studies, there was an increased incidence in fetal cardiovascular anomalies (especially ventricular septal defects). In the oral study, no maternal effects were seen at the highest dose tested (HDT) (30 milligrams/kilograms (mg/kg/day)); whereas, the effects in the fetuses were observed at 10 mg/kg/day. In the dermal study, no maternal effects were noted at the HDT (300 mg/kg/day); whereas, the effects in the fetuses were observed at 100 mg/kg/day. Regarding the 2-generation rat reproduction study, parental effects (red substance in vagina and increased mortality in females as well as decreases in male and female body weights, body weight gains, and food consumption) were noted at 18.9 mg/kg/day in males HDT and 22.7 mg/kg/day in females HDT. Based on the results of the study, no apparent reproduction effects were attributed to test article administration. The effects

observed regarding the offspring were a decrease in both the number of liveborn and pup body weights at 12.7 mg/kg/day for males and 15.1 mg/kg/day for females. Therefore, it was considered that there was both a quantitative and qualitative increase in susceptibility.

5. *Conclusion.* There is a complete toxicity data base for flumioxazin and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. The FQPA safety factor (as required by the Food Quality Protection Act of August 3, 1996) has been retained at 10x for all population subgroups for all exposure durations (acute and chronic) in assessing the risk posed by this chemical. The reasons for retaining the 10x safety factor are as follows. First, there is evidence of increased susceptibility of the rat fetuses to *in utero* exposure to flumioxazin by the oral and dermal route in the prenatal developmental toxicity studies in rats. In addition, there is evidence of increased susceptibility of young animals exposed to flumioxazin in the 2-generation reproduction toxicity study in rats. Finally, there is concern for the severity of the effects observed in fetuses and young animals when compared to those observed in the maternal and parental animals (dose- and treatment-related increase in the incidence of cardiovascular abnormalities, particularly ventricular septal defect, in the developmental studies; and decreases in the number of live born pups and pup body weights in the absence of parental toxicity in the reproduction study).

### D. 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 + chronic non-dietary, non-occupational exposure)]. This allowable exposure through drinking water is used to calculate a DWLOC.

A DWLOC will vary depending on the toxic endpoint, drinking water