

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 bifenthrin 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 as to bifenthrin and any other substances and bifenthrin 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 bifenthrin 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 Web site 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.* EPA concluded that there is not a concern for pre- and/or postnatal toxicity resulting from exposure to bifenthrin. There was no quantitative or qualitative evidence of increased susceptibility of rat or rabbit fetuses to *in utero* exposure to Bifenthrin in developmental toxicity studies and no quantitative or qualitative evidence of increased susceptibility of neonates (as compared to adults) to bifenthrin in a 2-

generation reproduction study in rats. In addition, there are no concerns or residual uncertainties for pre and/or post-natal toxicity following exposure to Bifenthrin.

3. *Conclusion.* No special FQPA safety factor is needed based on concerns for pre- and/or postnatal toxicity to bifenthrin. However, EPA has concluded that in light of the lack of the DNT study there is no reliable basis for removing the additional FQPA 10X safety factor when assessing acute (single dose) exposure scenarios. The following points were considered in this determination:

i. It is assumed that the DNT study will be conducted at dose levels similar to those used in the rat reproduction study with Bifenthrin wherein the offspring NOAEL was 5.0 mg/kg/day, the highest dose tested (no effects were observed in offspring at this dose); but that the DNT study would not be conducted at dose levels higher than 10 mg/kg/day since a range-finding study indicates excessive fetotoxicity occurred at this dose (all pups from 2 of the 4 litters at 10 mg/kg/day died within 14 days of birth).

ii. The DNT study may impact the currently selected acute regulatory dose since the NOAEL used to establish the acute Reference dose for dietary risk assessment is 33 mg/kg/day, a level which is more than 5-fold higher than the offspring NOAEL in the rat reproduction study of 5.0 mg/kg/day (a level which is similar to dose levels likely to be used in the DNT study).

EPA has further determined that for repeated dose exposure scenarios a 3X UF_{DB} is adequate to account for the lack of the DNT study. Repeated dose exposure scenarios include chronic dietary exposure; short-term (repeated exposure up to 30 days) and intermediate-term (repeated exposure from 1 to 6 months) incidental oral exposure; and short-term, intermediate-term, and long-term (several months to lifetime) dermal and inhalation exposure scenarios. EPA's determination that a 3X UF_{DB} is adequate for repeated dose exposure scenarios is based on the following considerations:

a. As stated above, the DNT study will likely be conducted at dose levels similar to the rat reproduction study.

b. The results of the DNT study are not expected to impact the current regulatory doses selected for repeated exposure scenarios since the NOAELs used for these risk assessment endpoints (e.g., 1.3 mg/kg/day from the chronic dog study for chronic RfD) are approximately 4-fold lower than the offspring NOAEL (5.0 mg/kg/day) in the

rat reproduction study conducted with Bifenthrin. Although the results of the DNT are not expected to impact the current regulatory dose given the 4-fold difference observed in the rat and dog studies, EPA does not have sufficient reliable data to apply no additional FQPA safety factor. Rather, EPA believes that the 4X difference between the offspring NOAEL in the rat reproduction study and the NOAELs used for risk assessment endpoints provides reliable data supporting a 3X UF for repeated dose exposure scenarios. The use of a 3X provides roughly a 10-fold difference between the NOAEL associated with the identified effects in the rat necessitating the DNT study and the NOAELs used for setting regulatory doses. Therefore, a UF_{DB} of 3X will be applied as a FQPA safety factor to repeated dose exposure scenarios to account for the lack of the DNT study with Bifenthrin.

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 are used to calculate DWLOCs: 2 liter (L)/70 kg (adult male), 2L/60 kg (adult female), and 1L/10 kg (child). Actual 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 ground water are less than the