

### 2. Prenatal and postnatal sensitivity.

Based on the available data, there is no quantitative and qualitative evidence of increased susceptibility observed following *in utero* pyriproxyfen exposure to rats and rabbits or following pre/postnatal exposure in the 2-generation reproduction study.

3. *Conclusion.* There is a complete toxicity data base for pyriproxyfen and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. EPA determined that the 10X safety factor to protect infants and children should be reduced to 1X because there was no evidence of prenatal or postnatal extra sensitivity or increased susceptibility in developmental studies in rats and rabbits, and in reproduction studies in rats. Likewise, there was no quantitative or qualitative evidence of increased susceptibility to rat or rabbit fetuses identified in the guideline prenatal developmental toxicity studies for rats and rabbits. Additionally, in the two non-guideline studies that evaluated perinatal and prenatal development, there was no evidence of quantitative or qualitative increased susceptibility. In one study, when pregnant rats were treated from gestation day 17 to lactation day 20, the resulting toxicity was comparable between adults (clinical signs, decreased body weight gain and food consumption) and offspring (decreased body weight and dilation of the renal pelvis) at the same dose. In the other study, when rats were exposed to pyriproxyfen prior to and in the early stages of pregnancy, no developmental toxicity was seen at the limit dose. Lastly, in the reproduction toxicity study, offspring toxicity (decreased body weight on pups during lactation days 14 to 21) occurred only in the presence of decreases in body weight in parental animals at the same dose level (i.e., comparable toxicity in adults and offspring).

### 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 estimated environmental 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 EPA Office of Water are used to calculate DWLOCs: 2 L/70 kg (adult male), 2 L/60 kg (adult female), and 1 L/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, OPP concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which OPP has reliable data) would not result in unacceptable levels of aggregate human health risk at

this time. Because OPP 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, OPP will reassess the potential impacts of residues of the pesticide in drinking water as a part of the aggregate risk assessment process.

1. *Acute risk.* An acute dietary RfD for females 13–49 and the general U.S. population, including infants and children, was not selected because an acute oral endpoint attributable to a single-dose exposure could not be identified in the toxicology data base, including maternal toxicity in the developmental toxicity studies. No acute dietary risk is expected.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to pyriproxyfen from food will utilize 1.1% of the cPAD for the U.S. population, 2.0% of the cPAD for all infants and 3.9% of the cPAD for children 1–2 years old. Pyriproxyfen is the active ingredient in many registered residential products for flea and tick control on pets and in the home for ant and roach control for indoor and outdoor applications. Based on the use pattern, the residential assessment was performed for toddlers since they are anticipated to have the higher chronic residential exposure to residues of pyriproxyfen. The total chronic food and residential aggregate MOEs range from 850 to 13,000. As these MOEs are greater than 100, the chronic aggregate risk does not exceed EPA's level of concern. In addition, there is potential for chronic dietary exposure to pyriproxyfen in drinking water. After calculating DWLOCs and comparing them to the EECs for surface and ground water, EPA does not expect the aggregate exposure to exceed 100% of the cPAD, as shown in Table 4 of this unit:

TABLE 4.—AGGREGATE RISK ASSESSMENT FOR CHRONIC (NON-CANCER) EXPOSURE TO PYRIPROXYFEN

Population Subgroup	Aggregate MOE (Food + Residential)	Target MOE	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Chronic DWLOC (ppb)
U.S. population	9,200	100	0.40	0.006	12,000
All infants	1,000	100	0.40	0.006	3,200
Children 1–2 years old	860	100	0.40	0.006	3,100
Children 3–5 years old	940	100	0.40	0.006	10,000