

Since the models used are considered to be screening tools in the risk assessment process, the Agency does not use estimated environmental concentrations (EECs) from these models to quantify drinking water exposure and risk as a percent of reference dose or percent of population adjusted dose. Instead, drinking water levels of comparison (DWLOCs) are calculated and used as a point of comparison against the model estimates of a pesticide's concentration in 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 from residential uses. Since DWLOCs address total aggregate exposure to cyprodinil they are further discussed in the aggregate risk sections below.

Based on the PRZM/EXAMS and SCIGROW models the estimated environmental concentrations (EECs) of cyprodinil for acute exposures are estimated to be 32 parts per billion (ppb) for surface water and 0.04 ppb for ground water. The EECs for chronic exposures are estimated to be 6 ppb for surface water and 0.04 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).

Cyprodinil 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 cyprodinil 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, cyprodinil 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 cyprodinil 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).

#### *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 of increased susceptibility of rat or rabbit fetuses following *in utero* exposure in the developmental studies with cyprodinil. There is no evidence of increased susceptibility of young rats in the reproduction study with cyprodinil.

3. *Conclusion.* With the exception of missing 21/28-day dermal toxicity and 28-day inhalation-toxicity studies in rats, there is a complete toxicity data base for cyprodinil and exposure data are complete or are estimated based on data that reasonably accounts for potential exposures. Since there are no residential uses for cyprodinil the only exposure route to infants and children is the oral route, for which the toxicity and exposure data base is complete. Therefore dermal and inhalation-toxicity studies, are not needed to assess risk to infants and children and EPA determined that the 10X safety factor to protect infants and children should be reduced to 1X.

The FQPA 10X safety factor is removed because:

- i. There are currently no registered or proposed residential (non-occupational) uses of cyprodinil.
- ii. There was no evidence (qualitative or quantitative) of increased susceptibility in the developmental rat or rabbit study following *in utero* exposure or in the two-generation reproduction study following pre- or post-natal exposure.
- iii. There was also no evidence of a neurodevelopmental effect in the rat or rabbit developmental toxicity studies or in the rat two-generation reproductive-toxicity study.

- iv. There are no data deficiencies for pre- and/or post-natal exposure and hence there are no residual uncertainties.

- v. Food and drinking water exposure assessments will not underestimate the potential exposure for all populations, including infants and children.

#### *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). 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, EPA concludes with reasonable certainty that exposures to the pesticide in drinking water (when considered along with other sources of exposure for which EPA has reliable data) would not result in unacceptable levels of aggregate human health risk at this time. Because EPA 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, EPA will reassess the potential impacts of residues of the pesticide in