

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 Indoxacarb they are further discussed in the aggregate risk sections below.

Based on the PRZM/EXAMS and SCIGROW models the estimated EECs of Indoxacarb for acute exposures are estimated to be 13.7 parts per billion (ppb) for surface water and 0.02 ppb for ground water. The EECs for chronic exposures are estimated to be 3.7 ppb for surface water and 0.02 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). Indoxacarb 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 Indoxacarb 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, Indoxacarb 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 Indoxacarb 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) (FRL-5754-7).

### 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.* There is no evidence for either qualitative or quantitative susceptibility. In all developmental studies, the developmental endpoint occurs at the maternal LOAEL or above. Although there is no rabbit developmental toxicity study with indoxacarb, a study is not required since:

i. Studies-both using methyl cellulose-comparing JW062 in the rabbit and rat demonstrate that the toxicity profiles for the rat and rabbit are similar and that the rat is the more sensitive species;

ii. Range finding studies in the rat comparing indoxacarb and JW062 indicate that the maternal and external developmental toxicity are comparable;

iii. A dietary developmental toxicity study in the rat with JW062 had comparable toxicity to the gavage indoxacarb rat developmental toxicity study. Developmental toxicity only occurred at levels at or above maternal toxicity.

The reproduction toxicity study with JW062 can be used to satisfy the requirement for an indoxacarb study because:

iv. Systemic toxicity is at similar doses and of similar magnitude to that observed in subchronic feeding studies with both indoxacarb and JW062;

v. based on the data base, the HIARC determined that there was support for using data from dietary studies conducted with JW062 to satisfy the data requirements for indoxacarb.

The Agency has required a developmental neurotoxicity study as confirmatory data due to:

- Clinical signs of neurotoxicity in several studies, males and females, mice and rats, at some doses that do not cause mortality;

- Signs of neurotoxicity in the acute neurotoxicity study-rat with indoxacarb (males and females), no mortality in males at neurotoxic doses;

- Clinical signs of neurotoxicity in the 90-day toxicity study-rat indoxacarb (females), mortality;

- Clinical signs of neurotoxicity in the 90-day toxicity study-mouse with the racemic mixture, JW062 (males and

females), no mortality in females at neurotoxic doses, mortality in males;

- Clinical signs of neurotoxicity in the 18 month carcinogenicity study-mouse with JW062 (males and females) high and mid dose, mortality at the high but no mortality at the mid dose; and

- Clinical signs of neurotoxicity in the developmental toxicity study-rat with JW062 (using methyl cellulose as the vehicle), at doses causing mortality.

3. *Conclusion.* The Agency concluded that the FQPA safety factor could be reduced to 1X for Indoxacarb because:

- There is no indication of quantitative or qualitative increased susceptibility of rats or rabbits to *in utero* and/or postnatal exposure;

- The requirement of a developmental neurotoxicity study is not based on the criteria reflecting special concern for the developing fetuses or young which are generally used for requiring a DNT study—and a safety factor (e.g.: neuropathy in adult animals; CNS malformations following prenatal exposure; brain weight or sexual maturation changes in offspring; and/or functional changes in offspring)—and therefore does not warrant an FQPA safety factor; and

- The dietary (food and drinking water) exposure assessments will not underestimate the potential exposures for infants and children

- There are no registered residential uses at the current time.

### 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 + 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 EPA's Office of Water are used to calculate DWLOCs: 2 liter (L)/70 kg (adult male), 2L/60 kg (adult female), and 1L/10 kg (child). Default