

- 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.

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 drinking water level of comparison (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 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 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 drinking water as a part of the aggregate risk assessment process.

1. *Acute risk.* Using the exposure assumptions discussed in this unit for acute exposure, the acute dietary exposure from food to Indoxacarb will occupy 12% of the aPAD for the U.S. population, 69% of the aPAD for females 13 years and older, 67% of the aPAD for infants less than 1 year old and 36% of the aPAD for children 1 to 2 years old. In addition, there is potential for acute dietary exposure to Indoxacarb 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 aPAD, as shown in Table 3 of this unit:

TABLE 3.— AGGREGATE RISK ASSESSMENT FOR ACUTE EXPOSURE TO INDOXACARB

Population Subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface Water EEC (ppb)	Ground Water EEC (ppb)	Acute DWLOC (ppb)
U.S. Population	0.12	7	13.7	0.02	3,700
Females 13 +	0.02	69	13.7	0.02	180
All infants less than 1 year	0.12	67	13.7	0.02	400
Children 1 to 2	0.12	36	13.7	0.02	760

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to Indoxacarb from food will utilize 30% of the cPAD for the U.S. population, 29% of the cPAD for infants less than 1 year old and 79% of the cPAD for children 1 to 2 years old.

There are no residential uses for Indoxacarb that result in chronic residential exposure to Indoxacarb. Based the use pattern, chronic residential exposure to residues of Indoxacarb is not expected. In addition, there is potential for chronic dietary exposure to Indoxacarb 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: