

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.* The developmental toxicity studies indicated no quantitative or qualitative evidence of increased susceptibility of rat or rabbit fetus to *in utero* exposure based on the fact that the developmental NOAELs are either higher than or equal to the maternal NOAELs. However, the reproductive studies indicate effects in male rats in the form of increased incidence and severity of testicular tubular atrophy. These data are considered to be evidence of increased quantitative susceptibility for male pups when compared to the parents.

3. *Conclusions.* Based on:

- i. Effects on endocrine organs observed across species.
- ii. The significant decrease in alanine amino transferase levels in the companion animal studies and in the dog studies.
- iii. The mode of action of this chemical in insects (interferes with the nicotinic acetyl choline receptors of the insect's nervous system) thus a developmental neurotoxicity study is required.
- iv. The transient clinical signs of neurotoxicity in several studies across species.
- v. The suggestive evidence of increased quantitative susceptibility in the rat reproduction study, the Agency

is retaining the FQPA factor which is 10X.

*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 + chronic non-dietary, non-occupational 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 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 ground water are less than the calculated DWLOCs, EPA concludes with reasonable certainty that exposures to thiamethoxam 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 thiamethoxam on 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 thiamethoxam will occupy 3% of the aPAD for the U.S. population; 2% of the aPAD for females 13 years and older; 7% of the aPAD for all infants <1 year old; and 9% of the aPAD for children 1–2 years old. In addition, despite the potential for acute dietary exposure to thiamethoxam in drinking water, after calculating DWLOCs and comparing them to conservative EECs of thiamethoxam in surface water and ground water, EPA does not expect the aggregate exposure to exceed 100% of the aPAD, as shown in the following Table 2:

TABLE 2.—AGGREGATE RISK ASSESSMENT FOR ACUTE EXPOSURE TO THIAMETHOXAM

Population subgroup	aPAD (mg/kg)	% aPAD (Food)	Surface water EEC (ppb)	Ground water EEC (ppb)	Acute DWLOC (ppb)
General U.S. population	0.1	3	7.1	1.94	3,400
All Infants (<1 year old)	0.1	7	7.1	1.94	930
Children (1–2 years old)	0.1	9	7.1	1.94	910
Children (3–5 years old)	0.1	6	7.1	1.94	940
Children (6–12 years old)	0.1	4	7.1	1.94	960
Youth (13–19 years old)	0.1	2	7.1	1.94	3,400
Adults (20–49 years old)	0.1	2	7.1	1.94	3,400
Adults (50+ years old)	0.1	2	7.1	1.94	3,400
Females (13–49 years old)	0.1	2	7.1	1.94	3,000

2. *Chronic risk.* Using the exposure assumptions described in this unit for

chronic exposure, EPA has concluded that exposure to thiamethoxam from

food will utilize 4% of the cPAD for the U.S. population, 8% of the cPAD for all