

i. Lack of concern for pre- and post-natal toxicity.

ii. No qualitative/quantitative evidence of increased susceptibility of rat or rabbit fetuses to in utero exposure was reported in the developmental studies at doses up to 1,000 mg/kg/day (limit dose) in the rat and 400 mg/kg/day (HDT) in the rabbit.

iii. There is no concern for developmental neurotoxicity resulting from exposure to imazapyr. While there were no neurotoxicity studies available from the published literature, there was no evidence of neurotoxicity/neuropathology in adult animals in the available studies.

iv. The toxicology database is complete based on the developmental studies in the rat and rabbit and the 2-generation reproduction study in the rat.

v. No developmental neurotoxicity (DNT) study was required.

vi. No residual uncertainties were identified in the exposure database.

vii. The chronic dietary food exposure assessment utilizes tolerance level residues and 100% CT information for all commodities. By using these screening level assumptions, actual exposures/risks will not be underestimated.

viii. The dietary drinking water assessment utilizes water concentration values generated by models and associated modeling parameters which are designed to provide conservative, health-protective, high-end estimates of water concentrations which will not likely be exceeded.

ix. Residential exposure and risk were assessed using standard assumptions from Science Advisory Council on Exposure (Expo SAC) Standard Operating Procedure (SOP). These

assumptions are not expected to underestimate risk.

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 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, the Office of Pesticide Programs (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.* No acute risk from exposure to imazapyr is expected because there were no toxic effects of concern attributable to a single dose identified in available data.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that exposure to imazapyr from food will utilize <1% of the cPAD for the U.S. population, <1% of the cPAD for all infants (<1 year old) and <1% of the cPAD for children ages 1–2 years old. Based the use pattern, chronic residential exposure to residues of imazapyr is not expected. In addition, there is potential for chronic dietary exposure to imazapyr 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 IMZAPYR.

Population Subgroup	cPAD (mg/kg/day)	Chronic Food Exposure (mg/kg/day)	Maximum Chronic Water Exposure ¹ (mg/kg/day)	Ground Water EEC ² ppb	Surface Water EEC ² ppb	Chronic DWLOC ³ ppb
U.S. Population	2.5	0.00034	2.499	1,700	81	87,000
All infants (< 1 year old)	2.5	0.000273	2.499	1,700	81	25,000
Children (1-2 years old)	2.5	0.000828	2.499	1,700	81	25,000
Children (3-5 years old)	2.5	0.00073	2.499	1,700	81	25,000
Children (6-12 years old)	2.5	0.000499	2.499	1700	81	75,000
Youth (13-19 years old)	2.5	0.000309	2.499	1,700	81	75,000
Adults (20-49 years old)	2.5	0.000267	2.499	1,700	81	87,000
Females (13-49 years old)	2.5	0.000257	2.499	1,700	81	87,000